The New England JOURNAL of MEDICINE

FORMERLY THE BOSTON MEDICAL AND SURGICAL JOURNAL

Official Organ of The Massachusetts Medical Society
The New Hampshire Medical Society — The Vermont State Medical Society
The New England Surgical Society — The Boston Surgical Society, Inc.
The New England Pediatric Society — The New Hampshire Surgical Club
The New England Obstetrical and Gynecological Society
And The Neisserian Medical Society of Massachusetts

OWNED AND PUBLISHED BY THE MASSACHUSETTS MEDICAL SOCIETY

211 Domestic $6 per Annum, 25c per Copy
6 Canada $7.04, Foreign $8.52

AUGUST 9, 1934

Published Weekly in Boston at 8 The Fenway

CONTENTS

THE MASSACHUSETTS MEDICAL SOCIETY

SECTION OF TUBERCULOSIS

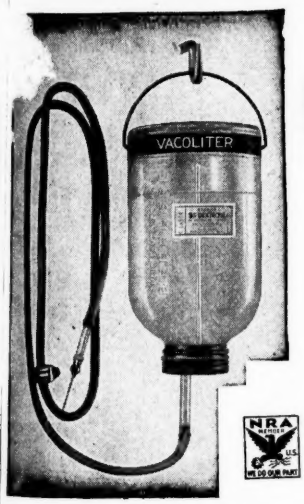
Symptoms as a Measurement of Tuberculous Activity. *Harvey S. Wagner*..... 237
Physical Signs as a Measure of Activity in Pulmonary Tuberculosis. *Frank H. Hunt*..... 239
The X-Ray in the Measurement of Activity in Pulmonary Tuberculosis. *Olin S. Pettingill.* 240
An Analysis of the Quantitative Tuberculin Test as an Index of Tuberculous Activity. *Theodore L. Badger* and *Walter K. Myers*..... 241
The Leucocytic Picture as an Aid in the Measurement of Activity in Pulmonary Tuberculosis. *Jacob Kaminsky*..... 245
The Monocyte-Lymphocyte Ratio as a Measurement of Activity in Pulmonary Tuberculosis. *Gulli Lindh Muller* and *Doris L. Davidson*..... 248
The Schilling Differential Count and Red Cell Sedimentation Rate as a Measurement of Activity in Pulmonary Tuberculosis. *John W. Cass, Jr.* and *Margaret Sutermeister*..... 252
Discussion and Summary of the Whole Problem with Especial Reference to the Study of the Leucocyte Count in Pulmonary Tuberculosis. *William H. Ordway*..... 260

NEW HAMPSHIRE MEDICAL SOCIETY

Phenobarbital Poisoning. *Bernard P. Haubrich.* 264
Bone Tumors. *Herbert L. Taylor*..... 267

Obstetrics in General Practice. A Review of 1000 Cases. *B. F. Macchia*..... 273

(Contents continued on next page)



BAXTER'S

INTRAVENOUS SOLUTIONS

(NON-PYROGENIC)

in

VACOLITER DISPENSERS

5% DEXTROSE (D-GLUCOSE) in distilled water	PHYSIOLOGICAL SODIUM CHLORIDE SOLUTION	10% DEXTROSE (D-GLUCOSE) in distilled water

5% and 10% Dextrose in water and Physiological Sodium Chloride Solution have been accepted by the Council on Pharmacy and Chemistry of the American Medical Ass'n.

Write for complete list and prices

Solutions of DEXTROSE (D-Glucose) and PHYSIOLOGICAL SODIUM CHLORIDE (Normal Saline) in Vacoliter Dispensers bring to the hospitals the definite advantages of Safety, Improved Service and Reduced Costs. ¶ Solutions prepared in Vacoliter Dispensers are non-pyrogenic—permitting rapid injection and increased dosage. ¶ Solutions in Vacoliter Dispensers are prepared from a fractionated, protein-free water, having an average Specific Electrical Conductivity of less than 1.0 x 10-6 mhos per cc. at 25° C. The pH value is always consistent with their concentration. Solutions in Vacoliter Dispensers are instantly available, as they are administered direct from the container. They are STABLE and sealed in vacuum and sterilized under recorded control. ¶ Baxter's non-pyrogenic solutions eliminate water distillation, filtration, sterilization, waste, overhead and expensive glassware. ¶ Vacoliter Dispensers of heavy Electroneal glass, when warmed, retain temperature; hence heating devices are not required in the average case.

Distributed in New England Exclusively by

E. F. MAHADY CO.

851-857 BOYLSTON STREET
BOSTON, MASS.

Entered at the Postoffice at Boston as Second Class Matter

CONTENTS

(Continued)

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Case 20321—J. H. Means and Tracy B. Mallory. Case 20322—Harold L. Higgins and Tracy B. Mallory 279

EDITORIALS

Education in Medicine and in Law 283
The Clinical Congress of the Connecticut State Medical Society 284
A Matter of Concern to the Medical Profession. 284
This Week's Issue 285

CORRESPONDENCE

Repudiation of a Book Review. William J. Robinson 286

MISCELLANY

Mortality Rates 278
Résumé of Communicable Diseases in Massachusetts for June, 1934 278

NOTICE OF MEETING 287

RECENT DEATHS 287

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES 288

The Massachusetts Medical Society

The next Annual Meeting of the Massachusetts Medical Society will be held in Boston, at the Hotel Statler, June 3, 4, and 5, 1935.

OFFICERS AND STANDING COMMITTEES ELECTED BY THE COUNCIL, JUNE 5, 1934

PRESIDENT: WILLIAM H. ROBEY, Boston.
VICE-PRESIDENT: PHILEMON E. TRUESDALE, Fall River.
SECRETARY: WALTER L. BURRAGE, Brookline.
TREASURER: CHARLES S. BUTLER, Boston.

STANDING COMMITTEES FOR 1934-1935

COMMITTEE OF ARRANGEMENTS
W. M. Shedden, *Chairman;* W. R. Morrison, Horatio Rogers, W. S. Burrage, R. P. Stetson.

COMMITTEE ON PUBLICATIONS
R. I. Lee, *Chairman;* Homer Gage, R. B. Osgood, R. M. Smith, F. H. Lahey.

COMMITTEE ON MEMBERSHIP AND FINANCE
D. N. Blakely, *Chairman;* Gilman Osgood, G. C. Caner, J. E. Fish, H. F. Newton.

COMMITTEE ON ETHICS AND DISCIPLINE
David Cheever, *Chairman;* W. D. Ruston, S. F. McKeen, A. C. Smith, R. L. DeNormandie.

COMMITTEE ON MEDICAL EDUCATION AND MEDICAL DIPLOMAS
Reginald Fitz, *Chairman;* C. H. Lawrence, C. A. Sparrow, E. S. Calderwood, A. S. Begg.

COMMITTEE ON STATE AND NATIONAL LEGISLATION
W. H. Robey, *Chairman;* T. J. O'Brien, F. E. Jones, A. W. Marsh, Shields Warren.

COMMITTEE ON PUBLIC HEALTH
Dwight O'Hara, *Chairman;* E. F. Cody, F. G. Curtis, Gerald Hoeffel, G. D. Henderson.

COMMITTEE ON MALPRACTICE DEFENSE
F. G. Balch, *Chairman;* E. D. Gardner, F. B. Sweet, R. P. Watkins, A. W. Allen.

COMMITTEE ON PERMANENT HOME: T. J. O'Brien, *Chairman;* S. B. Woodward, C. G. Mixter, J. M. Birnie, R. B. Greenough.

OFFICERS OF THE SECTIONS FOR 1935

ELECTED BY THE SECTIONS

(The street addresses may be obtained from the Annual Directory)

SECTION OF MEDICINE
Chairman, Francis M. Rackemann, Boston; *Secretary,* Richard P. Stetson, Chestnut Hill and Boston.

SECTION OF SURGERY
Chairman, Ralph W. French, Fall River; *Secretary,* E. Parker Hayden, Boston.

SECTION OF TUBERCULOSIS
Chairman, Donald S. King, Boston; *Secretary,* Olin S. Pettingill, Middleton.

SECTION OF PEDIATRICS
Chairman, Joseph Garland, Boston; *Secretary,* James M. Baty, Belmont and Boston.

SECTION OF OBSTETRICS AND GYNECOLOGY
Chairman, Thomas Almy, Fall River; *Secretary,* Charles J. Kickham, Brookline.

SECTION OF RADIOLOGY AND PHYSIOTHERAPY
Chairman, Franklin P. Lowry, Newton; *Secretary,* Philip H. Cook, Worcester.

SECTION OF DERMATOLOGY AND SYPHILOLOGY: *Chairman,* Charles J. White, Boston; *Secretary,* William P. Boardman, Boston.

OFFICERS OF THE DISTRICT MEDICAL SOCIETIES

ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR ANNUAL MEETINGS, BETWEEN APRIL 15 AND MAY 15, 1934.

(The street addresses may be obtained from the Annual Directory)

BARNSTABLE—*President,* J. L. Chute, Osterville; *Vice-President,* P. P. Henson, Hyannis; *Secretary,* J. I. B. Vail, Hyannis; *Treasurer,* H. B. Hart, Yarmouthport; *Librarian,* E. E. Hawes, Hyannis.

BERKSHIRE—*President,* W. P. Kelly, Pittsfield; *Vice-President,* R. J. Carpenter, North Adams; *Secretary,* H. J. Downey, Pittsfield; *Treasurer,* C. T. Leslie, Pittsfield.

BRISTOL NORTH—President, F. V. Murphy, Attleborough; *Vice-President,* L. E. Butler, Taunton; *Secretary,* C. B. Kingsbury, Taunton; *Treasurer,* J. V. Chatigny, Taunton.

BRISTOL SOUTH—*President,* Frank M. Howes, New Bedford; *Vice-President,* E. L. Merritt, Fall River; *Secretary-Treasurer,* Charles Shanks, New Bedford.

ESSEX NORTH—*President,* John Parr, Methuen; *Vice-President,* C. F. Warren, Amesbury; *Secretary-Treasurer,* E. S. Bagnall, Groveland.

ESSEX SOUTH—*President,* C. L. Hoitt, Lynn; *Vice-President,* G. E. Tucker, Salem; *Secretary,* R. E. Stone, Beverly; *Treasurer,* Andrew Nichols, III, Danvers; *Librarian,* C. M. Cobb, Lynn.

FRANKLIN—*President,* H. B. Marble, Shelburne Falls; *Vice-President,* W. J. Pelletier, Turners Falls; *Secretary-Treasurer,* Charles Moline, Sunderland.

HAMPDEN—*President,* A. J. Douglas, Westfield; *Vice-President,* T. S. Bacon, Springfield; *Secretary-Treasurer,* H. L. Smith, Springfield.

HAMPSHIRE—*President,* T. F. Corriden, Northampton; *Vice-President,* L. B. Pond, Easthampton; *Secretary-Treasurer,* F. E. O'Brien, Haydenville; *Librarian,* Jane B. Armstrong, Northampton.

MIDDLESEX EAST—*President,* J. H. Fay, Melrose; *Vice-President,* F. O West, Woburn; *Secretary,* K. L. Maclachlan, Melrose; *Treasurer,* Richard Dutton, Wakefield; *Librarian,* J. M. Wilcox, Woburn.

MIDDLESEX NORTH—*President,* F. R. Mahony, Lowell; *Vice-President,* E. O. Tabor, Lowell; *Secretary,* T. A. Stamas, Lowell; *Treasurer,* M. D. Bryant, Lowell; *Librarian,* P. J. Meehan, Lowell.

MIDDLESEX SOUTH—*President,* A. H. Blake, West Somerville; *Vice-President,* S. H. Remick, Waltham; *Secretary,* A. A. Levi, Cambridge; *Treasurer,* Edward Mellus, Newton; *Librarian,* N. A. Gallagher, Malden.

NORFOLK—*President,* Cadis Phipps, Brookline; *Vice-President,* L. F. Johnson, Norwood; *Secretary,* F. S. Cruickshank, Brookline; *Treasurer,* G. W. Kaan, Sharon.

NORFOLK SOUTH—*President,* F. A. Bartlett, Quincy; *Vice-President,* T. B. Alexander, Scituate; *Secretary-Treasurer-Librarian,* N. R. Pillsbury, South Braintree.

PLYMOUTH—*President,* L. A. Alley, Lakeville; *Vice-President,* W. T. Hanson, Bridgewater; *Secretary,* G. A. Moore, Brockton; *Treasurer,* A. C. Smith, Brockton; *Librarian,* J. H. Weller, Bridgewater.

SUFFOLK—*President,* R. L. DeNormandie, Boston; *Vice-President,* Conrad Wesselhoeft, Boston; *Secretary,* G. P. Reynolds, Boston; *Treasurer,* John Rock, Boston.

WORCESTER—*President,* E. B. Emerson, Rutland; *Vice-President,* W. F. Lynch, Worcester; *Secretary,* E. C. Miller, Worcester; *Treasurer,* E. P. Disbrow, Worcester; *Librarian,* A. C. Getchell, Worcester.

WORCESTER NORTH—*President,* C. B. Gay, Fitchburg; *Vice-President,* C. H. Jennings, Fitchburg; *Secretary,* F. M. McMurray, Fitchburg; *Treasurer,* F. H. Thompson, Jr., Fitchburg.

The New England
Journal of Medicine

VOLUME 211 AUGUST 9, 1934 NUMBER 6

The Massachusetts Medical Society

SECTION OF TUBERCULOSIS

Crystal Room, Hotel Bancroft, Worcester, Mass.
Wednesday, June 6, 1934, 9 A. M.

PRESIDING:
Dr. Roy Morgan, Westfield, Chairman.
Dr. Donald S. King, Boston, Secretary.

CHAIRMAN MORGAN: *Gentlemen*—The first business is the appointment of a Nominating Committee whose duty it is to nominate officers for this Section for next year. I nominate Doctors Pope, Pillsbury, and Holmes.

Is there any other business to be brought before the Section? If not, we will proceed with the regular program.

This year we have a symposium on the measurement of activity in pulmonary tuberculosis. We have seven of these papers, and let us hope that the papers will not exceed eight minutes each. We must be through by 12 o'clock.

The first paper is entitled "Symptoms." This is by Dr. Harvey S. Wagner, Barnstable County Sanatorium, Pocasset. Unfortunately, Dr. Wagner is sick and cannot be here to-day, but he sent a paper which will be read by Dr. Donald S. King, of Boston, our Secretary.

DR. DONALD S. KING: We are postponing all discussion until the end of the symposium.

SYMPTOMS AS A MEASUREMENT OF TUBERCULOUS ACTIVITY*

BY HARVEY S. WAGNER, M.D.†

SYMPTOMS in tuberculosis, as in any other disease, mean activity. They have always indicated it, since the earliest periods of medicine, when their systematic compilation was begun. This kind of evidence is most easily and quickly acquired. At a glance one can read a temperature pulse chart, note weight and get impressions of strength and well-being. Their degrees can be carefully evaluated after a few questions.

The so-called constitutional symptoms can be mentioned first. These will involve fever, fast pulse, weakness, emaciation, loss of appetite, and sweating. Of these, weakness, sweating, loss of appetite and weight generally appear first to be overcome as improvement occurs. The more these symptoms predominate, the more clearly does the pathological lesion stand out as being exudative.

One symptom, fatigue or sense of exhaustion, is markedly significant. If advanced cases do not lose it within a few weeks and if its nervous element can be ruled out, their condition generally proves to be desperate.

Inability to gain weight within a month's time, also loss of 30 per cent to 40 per cent of normal weight is immediately serious. In experiments on animals, emaciation in acute tuberculosis is found to be greater than in pneumonia or typhoid fever. Under conditions of rest, the absorption of toxemic products is reduced to a minimum and any patient retaining even meagre capacity to resist the disease is good for a gain of 20 per cent to 25 per cent of his loss. On the other hand, the ability to gain eight to twelve pounds over one's normal weight shows excellent resistance.

Regarding temperature, we are concerned with three main types, which give a general idea as to the nature of infection. When an afternoon fever is quite sustained 102° to 103°, with morning remissions of 1° to 2°, we think of a pneumonic type of activity. Such a fever persisting over a month we begin to consider hopeless.

An intermittent fever varying from subnormal in the morning to 102° at night becomes of grave significance after continuing two months. It is due not only to the absorption of toxins of the bacillus, but also to the absorption of broken-down tissue products of tubercles in advanced disease. Chills, sweating, great loss of weight and strength are associated with fever of this sort.

When fever falls to a benign type, there is no doubt that activity is lessening. When it falls to normal in the afternoon and evening, remaining there in spite of exercise, we may regard the case as quiescent or possibly as apparently arrested, providing there are no tubercle bacilli in the sputum and the x-ray and physical findings are consistent with those of a healed lesion. Aged tuberculous patients and fibroid cases must be scrutinized carefully, be-

*Read before the Section of Tuberculosis of the Massachusetts Medical Society, at its Annual Meeting, Worcester, June 6, 1934.

†Wagner, Harvey S.—Superintendent, Barnstable County Sanatorium. For record and address of author see "This Week's Issue," page 285.

cause even without fever, they are likely to carry progressive disease.

The typical pulse of tuberculosis is unstable and high in proportion to its accompanying fever. It is best to judge them together. A pulse rate over 85 in the male and over 90 in the female should suggest activity whether in diagnosis or in the reactivity of apparent arrest. In the diagnosed case, the unknown pulse is too variable and inconstant a factor to use alone as a base for diagnosis. While it is much more suggestive of activity in an apparently arrested case, even then with all other signals set against it, for example, normal temperature and an unchanged x-ray film, it will generally be practically disregarded.

Its chief help is to round out a good picture of tuberculous activity with other symptoms and to give a case with a low fever a bad prognosis.

There are three symptoms, i.e., cough, expectoration, and hemoptysis, that have to do with the presence of tubercles as they enlarge, become caseous, break down, and affect the smaller air passages. Dr. Allen K. Krause refers to them as catarrhal.

Cough is so much a part of a nervous reflex that in the beginning it, alone, cannot be depended upon to indicate a diagnosis because there are too many other conditions producing it.

After the diagnosis has once been made, we realize that the cough must have been a sign of activity in that particular case, weeks previously. It may be traced back in the history, so that according to the patient's statement it is the most frequent early symptom. However, I believe that a patient is often unaware of sputum in his throat, to the end that cough does not actually precede sputum so far in advance as his statement would lead us to infer. During the physical examination, it is customary in our clinic to instruct them to expectorate into a cup whatever arises in their throat after cough. As a result of this procedure, not infrequently it happens that a specimen with tubercle bacilli is found which the patient insists is the first yellow sputum he has ever raised. On the other hand, if an arrested case begins to cough again, his previous experience will lead him to apprehend sputum as soon as it appears.

Cough alone does not help much to indicate intensity of disease or its progress; nor would one be justified in throwing a case out of the apparently arrested column without a careful check-up of physical signs and x-ray data because of it.

The appearance of secretion with tubercle bacilli will make us consider the possibility of potential trouble, because the negative sputum cases of the apparent arrest column hold up much longer than the positive sputum cases in the quiescent column. In the latter, the danger of immediate extension of disease with positive sputum is considerable.

When hemoptysis occurs, it means advancing disease from the practical standpoint of rest treatment. It demands this to lessen activity that may follow immediately, and the possible extension of tubercles at a later date. It is so common in active pulmonary tuberculosis, that occurring at any later time, it is much easier to assume that the source of the hemoptysis was from an active tuberculous area and still harder to prove that it was from an inactive tuberculous area.

High authorities with wide experience do not view hemoptysis so pessimistically. Dr. Lawrason Brown says that while hemoptysis is not infrequently a sign of activity of the pathological process, its presence may not be of serious import, especially in women. Dr. Maurice Fishberg of New York is very optimistic, believing that so long as hemoptysis does not prove fatal immediately, it has very little effect on the disease and that activity should be judged by the constitutional symptoms at the time of its occurrence. Both of these men have access to a great amount of autopsy material in which the findings show that many cases going on to death following hemorrhage did so in the course of their disease rather than as the result of the hemorrhage.

Pleurisy is nearly always a secondary infection, probably connected with movement of bacilli in lymphatics from distant tubercles or from tubercles in the subadjacent parenchyma. When thoracic pains are actually due to pleurisy without constitutional symptoms, we would seem to be dealing with a low-grade type of infection. If there are too few organisms involved, there will be no constitutional response and the question regarding the cause of the symptom-pain will remain open. One does not worry much about pleurisy, because the general course of disease thereafter remains about the same notwithstanding it.

I used to believe that traction on adhesions produced pain, but we have stretched them frequently enough during the course of artificial pneumothorax treatment, with barely any sensation, that one ceases to blame them as formerly.

My conclusion is rather in the nature of an impression that constitutional symptoms measure tuberculous activity accurately, but that if they are lacking, as will frequently be found in the proliferative type of disease, it is so unsatisfactory to estimate it by the irregularly occurring symptoms associated with the growth and spread of tubercles, that one should resort to other measures.

CHAIRMAN MORGAN: The next paper will be "Physical Signs", by Dr. Frank H. Hunt, of the Boston Sanatorium, Mattapan.

PHYSICAL SIGNS AS A MEASURE OF ACTIVITY IN PULMONARY TUBERCULOSIS*

BY FRANK H. HUNT, M.D.†

IN this paper I will state my conclusions in the beginning. These are, first, that as a measure of activity, physical signs alone are at all times inadequate, and secondly, are very often absolutely misleading. They are specific in base fluids, however.

To bring out these points more explicitly, I wish to cite a few cases. In these, we had previously correlated our physical signs and x-ray findings and had arrived at a conclusion as to the location, extent and character of the lesion. We had classified them and had taken into consideration that they were caseous, fibro-caseous or fibroid in type.

It is an observed fact, that, with progressive improvement or decline in our patient, many of our original signs clear up on the one hand, or increase on the other. Unfortunately, too many cases present themselves in which we find a clearing up of the original process and a corresponding improvement in our patient, but the radiogram, while agreeing with our physical findings thus far, reveals a new infiltrative lesion in another part of the lung.

The reverse of this picture may be true though not so frequently.

CASE 1 is that of a twenty-three year old girl, who had entered the sanatorium with an infiltrative process of the right upper lobe and a minimal lesion of the left apex. She had the usual symptoms of loss of weight and strength, cough with positive sputum, temperature and pulse elevated. Six months later she had gained twenty-five pounds, lost her positive sputum, and her temperature and pulse had become normal.

After remaining symptom-free for the next twelve months, she was examined with the idea of discharging her to her home and back to work. At this time she showed a remarkable clearing of her right upper lesion, with an x-ray reading of fibrosis. The minimal lesion in the left apex showed no increase. There were no symptoms.

She was advised as to her excellent progress, that she was practically well, but that she should continue sanatorium life for another six months making assurance doubly sure. At the end of this time the physical signs were exactly the same as on previous examination, symptoms absent, but on x-ray showed a very definite infiltration, of sizable degree, extending outward from the hilus of the better lung. A reëxamination gave us no indication of this new lesion.

It may interest Dr. Cass to know that the sedimentation rate was high at the time we advised her to stay six months longer, and before the last x-ray referred to.

CASE 2 was discharged against advice in 1928. Her physical examination at that time elicited moderate dullness, bronchial breathing, whispered and spoken voice increased in the upper half of the left chest with coarse moist râles extending down to the base. Sputum was positive, weight 125 lbs. Temperature and pulse normal. She felt very well with the exception of a slight cough and expectoration. There were no apparent symptoms. She said she was "fed up" on sanatorium routine and could not be persuaded to continue treatment.

She went home, rested for a few months and then took a clerical position, working from nine till five. She kept good hours and rested when off duty, but had had no time off for sickness.

Upon a check-up six years after her discharge, a physical examination showed the same findings as in 1928. She had been having her sputa examined about once a month and it had remained consistently negative for the past four years. She weighed 135 pounds. An x-ray showed a most striking dissemination of calcified tubercles, which is to me a most wonderful example of just how much physical signs may mislead us. Certainly, even now, this girl would have to go on absolute rest if physical signs were to be a gauge of her T.B. activity.

CASE 3. One of the Cabot Case Records that was published in the *New England Journal of Medicine* of March 8, 1934, was that of a fifty-one year old woman, giving a history of bronchial asthma of thirty-five years' duration. Here we have a diagnosis of tuberculosis based on doubtful physical findings, doubtful x-ray interpretation, negative sputum and normal temperature. The blood picture and blood pressure, at least, suggested a non-tuberculous condition.

I would like to say a word about chest signs and non-tuberculous complications. It seems to me that too little consideration is being given to the treatment of these conditions, when in fact they are so often the only real basis of the patient's indisposition.

Within the last few weeks we have had referred to us a patent case of obstructive jaundice, progressive infectious arthritis, esophageal stricture, hypertension and chronic myocarditis. These are all negative sputum cases with vague chest signs and x-ray evidence of some possible tuberculous condition. While it is the duty of sanatoria to treat these complications, it is assuredly not their place to take such patients, based upon the fear that they may develop active tuberculous disease later.

I do not wish to create the impression that physical signs are of no value. They have their own particular worth in diagnosis and it is becoming more and more evident that too little, rather than too much, stress is being placed upon them. Their neglect means more work and less intelligent interpretation for the examiner.

CHAIRMAN MORGAN: Our next paper is entitled "X-Ray", by Dr. Olin S. Pettingill, Essex County Sanatorium, Middleton.

*Read before the Section of Tuberculosis of the Massachusetts Medical Society, at its Annual Meeting, Worcester, June 6, 1934.

†Hunt, Frank H.—Resident Medical Officer at the Boston Sanatorium. For record and address of author see "This Week's Issue," page 285.

THE X-RAY IN THE MEASUREMENT OF ACTIVITY IN PULMONARY TUBERCULOSIS*

BY OLIN S. PETTINGILL, M.D.†

THIS discussion is limited to the evaluation of shadows cast on the x-ray film by certain pulmonary lesions and to the type of pathology they indicate. The information conveyed by one flat film or by well-taken stereoscopic films is of far less value than serial films in the same proportion as a complete physical examination of a patient is to the observation of that patient in a known environment. The interpretation of x-ray films will always remain more or less empirical, but with the accumulation of reliable data, the usual course of events can be foretold with greater accuracy. The value placed on the roentgenogram in the study of activity of resident cases at Essex Sanatorium is shown by the increase in the number of serial x-rays taken each year. Ten years ago, the average was one film per patient every ten months; last year, the average was one film per patient every four months. The x-ray film shows the extent and type of lesion with some suggestion as to the duration of disease and the degree of pathological activity present. The correlation of the shadows on the x-ray film, with physical signs, laboratory findings, complications, age, sex and constitutional disturbance is necessary to complete the interpretation.

The three chief types of reaction to tuberculous infection are progression without healing, progression with healing, and retrogression without extension.

Pathological activity has been defined as "that condition of a tuberculous process in which reaction on the part of the tissue cells accompanied by changes of a progressive nature is taking place[1]".

It is not within the scope of this paper to describe in detail the pathology of pulmonary tuberculosis, but we are all familiar with the word picture of the acute process when seen in the lung parenchyma, which consists of a central area of necrosis enveloped by cellular hyperplasia and lymphoid infiltration, and the whole surrounded by vesicular hepatization[2]. The shadow produced on the x-ray film by such pathology has a relatively dense central portion which gradually fades peripherally into normal lung density. This type of lesion has been variously described as fluffy, nebulous, flocculent, or of the "cotton ball" appearance of Sampson.

*Read before the Section of Tuberculosis of the Massachusetts Medical Society, at its Annual Meeting, Worcester, June 6, 1934.

†Pettingill, Olin S.—Superintendent, Essex County Sanatorium. For record and address of author see "This Week's Issue," page 285.

CAVITY

Allen[2] states that ring shadows after excluding bronchiectasis in patients with positive sputum, must be considered cavities. It is possible for an apical cavity to be entirely "walled off" by dense fibrous tissue, become inactive, and remain so for years. If a fluid level can be demonstrated in a rarefied area, which changes with the position of the patient, and in serial x-rays varies in height, interpreted as filling and emptying with inflammatory exudates, the cavity must be considered active regardless of the abruptness of the surrounding peripheral shadow.

HEALING OR RETROGRESSION

When healing or retrogression occurs, there is reabsorption of the exudation, organization, fibrous tissue ingrowth, and contraction with possibly the precipitation of calcium within the central contracting mass. The entire lesion may become surrounded in the end by perfectly normal air cells[2]. The x-ray reveals this process by the shadow becoming more dense, with or without linear markings, the periphery assuming a more abrupt delineation until a dense shadow with a sharp margin is seen. If this acute lesion is small, it may entirely disappear from detection by the x-ray film. Just when a healing process ceases to be active is often impossible to determine. Border-line lesions offer a fertile field for speculation. Retrogression may cease at any time, or evidence of spread may unexpectedly appear depending in many instances on other conditions than exist within the lung.

SPREAD OR PROGRESSION

When progression or reactivity of disease occurs, the existing lesions usually increase in size with or without new foci. The borders of these shadows have the characteristic hazy appearance of pathologically active lesions which is caused by perifocal inflammation and hyperemia. In addition, rarefied areas, interpreted as cavities, may appear and increase in size, or a group of small cavities may become one large cavity. In a series of nineteen cases studied at Essex Sanatorium by Weisman, reactivation of disease was first noticed on the x-ray film by peripheral spread of existing areas in 79 per cent. Changes may take place in the presence of large areas of disease, which the x-ray will not reveal because they are hidden by the massive lesion.

EARLY X-RAY EVIDENCE OF PATHOLOGICAL ACTIVITY

The x-ray usually reveals the presence of pulmonary tuberculosis and the progress of the disease earlier than physical signs or symptoms. In an attempt to determine how soon tubercles appeared upon the film, Sampson and Brown[3] studied by x-ray miliary tuberculosis in rabbits and have seen definite tubercles on the film thirteen days after inoculation. In a group of 103 cases diagnosed as pulmonary tuberculosis at our out-patient clinic, 60 per cent classified as minimal and 13 per cent of the moderately advanced revealed no physical signs. The presence of râles after the x-ray reveals an arrested lesion, or little if any pathology is common in our experience. Râles occasionally occur and spread after the x-ray shows retrogression. Zacks[5] in a study of 110 school children, found that râles appeared on an average of 2.6 years after the x-ray demonstrated the lesion while symptoms appeared, on an average, three years after x-ray evidence.

RELAPSE OF EXACERBATION

In ninteen cases of exacerbation of disease at Essex Sanatorium, the x-ray revealed spread before symptoms occurred in a little less than one-half of the instances. Pirie[4] stated that from the observation of 141 tuberculous soldiers over a period of three and a half years, the x-ray findings were "well in advance" of the clinical in the case of either progression or retrogression of the disease. The superiority of the x-ray in determining activity of disease in contrast to clinical methods has been shown by Sampson and Brown in a study of the progress of 373 patients during their sanatorium residence. When the disease was clinically inactive on admission, 17 per cent grew worse compared with only 6 per cent for the x-ray inactive group.

ARRESTED LESIONS

The lesion that appears on the film as a dense shadow with a clear-cut, abrupt margin, sometimes isolated and showing no change over a period of years, may be considered arrested. To infer that such a lesion is healed, we must assume that it does not harbor virulent tubercle bacilli which is beyond what may be deducted from any x-ray observation.

REFERENCES

1 Duffy, John: Activity in pulmonary tuberculosis as determined by a comparative study of roentgenograms, blood sedimentation and leucocytic reactions. Tubercle. 14:60 (Nov.) 1932 and 14:113 (Dec.) 1932.
2 Allen, L. G.: The radiographic evaluation of the pulmonary tuberculosis lesions. J. Kansas M. Soc. 26:211 (July) 1926.
3 Sampson H. L., and Brown, L.: The value of the roentgenologic examination in pulmonary tuberculosis. Am. J. Roentgenol. 25:209 (Feb.) 1931.
4 Pirie, A. H.: Prognosis in tuberculosis of the lungs from examination by the x-rays. Am. J. Roentgenol. 10:366, 1923.
5 Zacks, D.: What we have learned in Massachusetts from the ten-year program. New Eng. J. Med. 205:525 (Sept. 10) 1931.
6 Weisman, J. J.: Study of Records at Essex Sanatorium.

CHAIRMAN MORGAN: The next paper is "Quantitative Tuberculin Tests", by Dr. Theodore L. Badger and Dr. Walter K. Myers, Boston City Hospital.

AN ANALYSIS OF THE QUANTITATIVE TUBERCULIN TEST AS AN INDEX OF TUBERCULOUS ACTIVITY*

BY THEODORE L. BADGER, M.D.,† AND WALTER K. MYERS, M.D.†

WHAT is the status of the quantitative tuberculin test, may be asked with some justification. Constantly earlier diagnoses of tuberculosis are being made, and some refinement of laboratory procedures whereby we may estimate the activity or inactivity of the tuberculous process is highly desirable. We will discuss the reactions to measured dilutions of tuberculin in individuals with known, healed or active pulmonary tuberculosis and in normal controls.

No attempt is made to review the voluminous literature on various aspects of tuberculin tests and their interpretation. It is thought that the tuberculin test may be an indication of tuberculous infection[1, 2] with no relation to its anatomical extent in the lung or elsewhere, and that it bears a questionable relation to the degree of activity of the process itself. Chadwick[3], testing 42,000 school children in Massachusetts, found 28 per cent reacting positively but only 1.5 per cent with childhood type of tuberculosis demonstrable. Schwartz and Heise[4] showed little relationship between reactivity to tuberculin and the activity of the tuberculous process. Various authors, Blair[5], Dickey[6], Atsatt[7] and King[8] have indicated the desirability of an accurate quantitative tuberculin test to gauge activity of the tuberculous process. These authors seem to admit that the response to tuberculin is an indication of tissue hypersensitivity as the result of tuberculous infection and, at the same time, accept the test as a measure of tuberculous activity. They attempt to fix a definite tuberculin dilution as a critical threshold above which a patient with a positive reaction may be said to have an active process. But these studies have not been carried out with what appears to be adequate diagnostic equip-

*From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard), the Boston City Hospital, the Department of Medicine, Harvard Medical School, and the Channing Home for Tuberculosis, Boston, Mass.
Read before the Section of Tuberculosis of the Massachusetts Medical Society, at its Annual Meeting, Worcester, June 6, 1934.

†Badger, Theodore L.—Research Fellow, Thorndike Memorial Laboratory, Boston City Hospital. Myers, Walter K.—Resident Physician, Thorndike Memorial Laboratory, Boston City Hospital. For records and addresses of authors see "This Week's Issue," page 285.

ment or with a sufficiently long period of observation to be convincing.

It is hoped that this present study will in some way contribute to an estimate of what can be measured by the quantitative tuberculin test; namely, whether it is the degree of activity of the underlying tuberculous process or the degree of tissue hypersensitivity developed by the infection.

Two groups of a total of 207 women have been tested and studied with respect to tuberculin reactions. One was a group of 161 female nurses between the ages of eighteen and twenty-five years, in the training school of the Boston City Hospital during the past two years. Each individual on admission had a routine tuberculin test, a complete history, a general physical examination and a stereoscopic x-ray examination of the lungs. The tuberculin test and x-ray examination have been repeated annually.

The second group similarly studied consisted of forty-six female patients with known pulmonary tuberculosis at the Channing Home in Boston. All of these latter patients were under observation for three months or longer.

The tuberculin used in all tests was Saranac tuberculin.* Fresh dilutions were carefully prepared from the stock concentrate. All dilutions of tuberculin were cultured for sterility before use. All tests were made and read by the authors.

The technique employed in testing was the Mantoux Test, i.e., intradermal injection of 0.1 cc. of measured dilutions of tuberculin. The inner aspect of the forearm was always the site of injection. Readings were made forty-eight hours after injection, and interpreted as a 1, 2, 3, and 4 plus according to the standards of the National Tuberculosis Association[9]. Edema, visible or palpable but not exceeding 10 mm. in diameter at the site of inoculation has been the criterion of a positive or 1 plus reaction. Redness without edema has been interpreted as negative.

THE RESULT OF TUBERCULIN TESTS ON NURSES IN TRAINING AT THE BOSTON CITY HOSPITAL. The first three classes of nurses on admission were tested with tuberculin dilutions of 1:1,000 and, if negative, 1:100. Reactions to the 1:1,000 dilution were severe in many cases. Because of this, it was felt that a finer interpretation of reactions could be obtained with higher dilutions of tuberculin. Consequently, the nurses were given simultaneous intracutaneous tests of 0.1 cc. each of 1:40,000, 1:20,000, and 1:10,000 dilutions respectively. If negative these were followed by a 1:1,000 dilution and a 1:100 if necessary. But once again, many severe reactions were obtained in this group tested with higher dilutions. Thereafter, we adopted the routine of an initial test of 0.1 cc. of a 1:100,000 dilution. If negative, this was followed in succession by a 1:20,000, 1:1,000, and 1:100 dilution to the point where a positive reaction was obtained. All nurses who remained in training were tested with this routine. On this basis a reaction to tuberculin of a 2 plus or greater was rare. The highest dilution to which an individual responded with a positive reaction is the one recorded in all tables. No dilutions more concentrated than 1:100 were used and those not reacting to this were considered negative.

With these four dilutions, 161 nurses in training were tested, some of whom had been in training two years. Table I shows the result of the reactions in these 161 nurses so tested.

TABLE I

RESULTS OF QUANTITATIVE TUBERCULIN TESTS IN 161 NURSES. (BOSTON CITY HOSPITAL.)

	Positive					Negative
Dilution	1:100,000	1:20,000	1:1,000	1:100	Total	All Dilutions
Number Reacting	17	38	37	9	101	60
Per Cent Reacting	10.6	23.6	22.9	5.6	62.7	37.3

Of the 101 positive tuberculin reactors, 81 or 80.2 per cent represented nurses in whom no tuberculous lesion could be demonstrated. Eighteen, or 17.8 per cent, had fibrotic or calcified lesions. Two nurses presented evidences of an active tuberculous infection. Of the 101 individuals reacting positively, 55 or 54.5 per cent did so to a dilution of 1:20,000 or higher. Among those nurses reacting to dilutions of 1:20,000 or higher there were 13 with healed tuberculous lesions (9 calcified and 4 fibrotic) and 2 with an active tuberculous process. In the remaining 45.5 per cent who reacted only to the lower dilutions of 1:1,000 or 1:100 there were only 5 individuals with healed lesions (4 calcified and 1 fibrotic).

The 13 nurses with calcified lesions and the 5 with fibrotic lesions have remained in training with no demonstrable change in their process by x-ray or clinical signs suggestive of activity.

TABLE II

RESULTS OF POSITIVE TUBERCULIN TESTS IN THIRTEEN NURSES WHO SHOWED CALCIFIED LESIONS AND FIVE NURSES WHO SHOWED FIBROTIC LESIONS.

Dilution	1:100,000	1:20,000	1:1,000	1:100
Calcified Lesions	1	7	3	2
Fibrotic Lesions	0	4	1	0
Total	1	11	4	2

*Human tuberculin of standard strength and potency was prepared in concentrate by Mr. George Hulpritt, Saranac Lake, N. Y.

The tuberculin reactions of these 18 with healed lesions are shown in table II.

Thus, 12 out of the 18 individuals with healed lesions or 66.6 per cent showed a reaction to the dilutions of 1:20,000 or above. Only 33.3 per cent of those individuals with healed lesions reacted in the lower dilutions alone.

The 81 positive reactors in whom no tuberculous lesion could be found responded as shown in table III.

TABLE III

DISTRIBUTION OF POSITIVE TUBERCULIN TESTS IN EIGHTY-ONE NURSES IN WHOM NO TUBERCULOUS LESION COULD BE FOUND

Dilution	1:100,000	1:20,000	1:1,000	1:100
Number	16	27	31	7
Per Cent	19.7	33.3	38.2	8.7

Here, also, in 43 out of 81, or 53 per cent of the nurses with no demonstrable lesions, a positive reaction to the higher dilutions was observed. None of these individuals have developed any clinical or x-ray evidence of tuberculosis.

Among the 60 individuals who failed to give positive reactions there were two with calcified mediastinal glands probably from an early childhood infection. It is noted, however, that those two with active lesions both reacted to the dilution of 1:20,000.

THE RESULTS OF TUBERCULIN TESTS IN 46 PATIENTS WITH KNOWN PULMONARY TUBERCULOSIS AT THE CHANNING HOME. The same tuberculin and technique in testing and interpretation were used with these patients as with the former group of nurses. It proved unnecessary to do any tests with the 1:100 dilutions of tuberculin, as none failed to react to the 1:1,000 dilution.

All of these patients were known to have pulmonary tuberculosis either because of tubercle bacilli in their sputum or repeated x-ray examinations with a clinical picture characteristic of the disease. For the sake of simplicity the results of these quantitative tuberculin tests are presented in three aspects: (a) according to the anatomical extent of the process in the lungs, namely, minimal, moderately advanced, and far-advanced lesions; (b) according to symptoms, slight or none, moderate and severe; and (c) according to the status of the tuberculous process; arrested, quiescent, improved or unimproved. This classification is based on the standards for each group as outlined by the National Tuberculosis Association[9].

The results according to the anatomical extent of the lesions in the lungs are shown in table IV.

This table is self-explanatory and shows no consistent correlation between the quantitation of tuberculin reactions and the size of the lesion in the lungs.

The results according to symptoms are shown in table V.

Here again, there is very little consistency in the reactions. No correlation of the response to a known dilution of tuberculin with symptoms is apparent. The group with slight or no symptoms and the group with severe symptoms show the reverse of what would be expected if quantitative tuberculin tests are in any way an index of tuberculous activity. Nineteen of 31 in the group with slight symptoms respond to high dilutions of 1:20,000 and above. Neither of two patients with severe symptoms responded to high dilutions.

TABLE IV

THE RELATION OF QUANTITATIVE TUBERCULIN TESTS TO ANATOMICAL EXTENT OF THE TUBERCULOUS LESION IN THE LUNG. (THE CHANNING HOME FOR TUBERCULOSIS.)

Dilution	Minimal	Mod. Advanced	Far Advanced
1:100,000	3	2	4
1:20,000	5	5	8
1:1,000	5	4	10
1:100	—	—	—
Total	13	11	22

TABLE V

THE RELATION OF QUANTITATIVE TUBERCULIN TESTS TO SYMPTOMS

Dilution	Slight or None	Moderate	Severe
1:100,000	7	2	0
1:20,000	12	6	0
1:1,000	12	5	2
1:100	—	—	—
Total	31	13	2

Results according to the status of the underlying process as determined by sputum, x-ray examination and symptoms of the patient are shown in table VI.

TABLE VI

THE RELATION OF QUANTITATIVE TUBERCULIN TESTS TO THE STATE OF ACTIVITY OF THE TUBERCULOUS PROCESS

Dilution	Arrested	Quiescent	Improved	Unimproved
1:100,000	3	4	0	2
1:20,000	1	7	8	0
1:1,000	1	6	12	2
1:100	—	—	—	—
Total	5	17	20	4

Here the reactions to the highest and lowest dilutions in the "arrested" and "quiescent" cases are evenly divided, as in the group of "unimproved" patients. The quantitative tuberculin test again shows no correlation with the degree of activity of the tuberculous process.

DISCUSSION

Two points were brought out by the reactions of these two groups of individuals to measured quantities of tuberculin.

There was no consistent correlation between the quantitative tuberculin test and the activity or inactivity of the tuberculous process. There was no tendency for patients with old healed or arrested lesions to react only to the lower dilutions, or for the patients with the newer active and progressive lesions to give a response only to higher dilutions of tuberculin. No critical threshold of tuberculin dilution could be found which could be considered an index of tuberculous activity. The quantitative tuberculin test is not a laboratory procedure of precision or value in detecting activity in tuberculosis.

It does seem, however, that the quantitative tuberculin test is an important measure of allergy, i.e., the degree of tissue hypersensitivity. Rich[10, 13] has shown that immunity may exist in the absence of allergy and that these two phenomena may be experimentally dissociated. Activity in the tuberculous process, as in other infections, may depend on the degree of immunity, but its relation to allergy is not so clear[11, 12]. Very little is known regarding the influence of hypersensitivity on tuberculous lesions or what alterations in the degree of hypersensitivity may occur in the same patient over long periods of time or under altered physiological conditions. Rothschild[14] has experimentally desensitized immune animals to tubercle bacilli and tuberculin, without novel changes in the tissues of the animal. Clinically, the quantitative tuberculin test appears to be an index of the degree of tissue hypersensitivity in response to tuberculous infection. Further studies with measured dilutions of tuberculin, carefully controlled, may contribute much valuable information regarding the influences which alterations in tissue hypersensitivity exert on tuberculous infection.

It would appear from this study that the quantitative tuberculin test is a measure of the degree of tissue hypersensitivity dependent on the presence of tuberculous infection rather than the degree of activity of the tuberculous process itself.

CONCLUSIONS

1. A total of 207 individuals have been tested with measured dilutions of tuberculin to determine what relation, if any, exists between the reaction to such measured dilutions and the nature of the tuberculous process in the lung.

2. Two controlled groups were studied. One was a group of 161 female nurses in training and the other was a group of 46 tuberculous women.

3. Measured dilutions of 1:100,000, 1:20,000, 1:1,000 and 1:100 were used throughout. In addition to the tuberculin tests a thorough history, general physical examination and repeated stereoscopic x-ray examination of the lungs were obtained in every case.

4. All individuals were under observation for from three months to two years.

5. The individual response to measured dilutions of tuberculin bore no consistent relation to the activity or inactivity of the tuberculous process.

NOTE: The authors thank the Matron's Office, the Out-Patient Staff, and the Roentgenologists of the Boston City Hospital, as well as the Nursing Staff of the Channing Home, for their help and coöperation in making this study possible. They also appreciate the assistance of Miss Sweet, in the Biological Laboratory of the Children's Hospital, and of Miss M. Jewell of the Thorndike Memorial Laboratory for their technical assistance in the preparation of the tuberculin dilutions.

REFERENCES

1 Moncrieff, A.: The clinical interpretation of the intradermal tuberculin reaction. Quart. J. Med. 24:153 (Jan.) 1931.
2 Chadwick, A. E.: Current opinions of the tuberculin reaction and its interpretation. Am. Med. 26:649 (Dec.) 1931.
3 Chadwick, H. D., and Zacks, D.: The incidence of tuberculous infection in school children. New Eng. J. Med. 200:332 (Feb. 14) 1929.
4 Schwartz, W. S., and Heise, F. H.: Variations in tuberculin sensitiveness in tuberculosis patients. Am. Rev. Tuberc. 24:479 (Oct.) 1931.
5 Blair, J. E., and Galland, W. I.: A quantitative tuberculin test. J. Lab. & Clin. Med. 15:566 (March) 1930.
6 Dickey, L. B.: The size of the reacting area in intracutaneous tuberculin tests in relation to classification of disease and to other clinical factors. Am. J. Dis. Child. 38:1155 (Dec.) 1929.
7 Atsatt, R. F.: Studies with a quantitative tuberculin reaction. J. Bone & Joint Surg. 9:657 (Oct.) 1927.
8 King, R. B.: A tuberculin test of value in adults. New Eng. J. Med. 207:831 (Nov. 10) 1932.
9 National Tuberculosis Assoc. Diagnostic Standards, Jan., 1931.
10 Rich, A. R., Jennings, F. B., Jr., and Downing, L. M.: The persistence of immunity after the abolition of allergy by desensitization. Bull. Johns Hopkins Hosp. 53:172 (July) 1933.
11 Rich, A. R., and McCordock, H. A.: Enquiry concerning rôle of allergy, immunity and other factors of importance in the pathogenesis of human tuberculosis. Bull. Johns Hopkins Hosp. 44:273 (May) 1929.
12 Rich, A. R., Chesney, A. M., and Turner, T. B.: Experiments demonstrating that acquired immunity in syphilis is not dependent upon allergic inflammation. Bull. Johns Hopkins Hosp. 52:179 (March) 1933.
13 Rich, A. R., and Brown, J. H.: Dissociation of allergy from immunity in pneumococcus infection. Proc. Soc. Exper. Biol. & Med. 27:695, 1929-30.
14 Rothschild, H., Friedenwald, J. S., and Bernstein, Clarence: The relation of allergy to immunity in tuberculosis. Bull. Johns Hopkins Hosp. 54:232 (April) 1934.

DISCUSSION

CHAIRMAN MORGAN: Before we go on with the program, the Nominating Committee has submitted the following names for officers for this Section for next year: Dr. Donald S. King, Boston as Chairman; and Dr. Olin S. Pettingill, Middleton, as Secretary. What is to be done with the nominations?

Well, if there are no other nominations, the Secretary will cast one ballot, and these two men nominated are hereby elected.

Our next paper is on the "Leucocytic Picture", by Dr. Jacob Kaminsky, Middlesex County Sanatorium, Waltham.

DR. JACOB KAMINSKY: *Mr. Chairman, Ladies and Gentlemen*—I feel that to present my material on this subject in the presence of Dr. Ordway from Mt. McGregor is like carrying coals to Newcastle. They have done a great deal of work at Mt. McGregor and are pioneers in this line. My only justification is the fact that very few men engaged in clinical work have followed the lead of Mt. McGregor, and I may, perhaps, bring out a point or so that will prove of some interest.

THE LEUCOCYTIC PICTURE AS AN AID IN THE MEASUREMENT OF ACTIVITY IN PULMONARY TUBERCULOSIS*

BY JACOB KAMINSKY, M.D.†

REFERENCES to the value of the leucocyte count in tuberculosis may be found in publications by the older writers. However, our more recent knowledge of the application of the leucocytic picture in the study of tuberculosis is derived largely from the work of Medlar and his associates and Cunningham and Sabin and their co-workers. The latter have acquainted us with the rôle of the monocyte in tuberculosis and they have stressed the clinical significance of the monocyte lymphocyte ratio in the peripheral blood in this disease[1]. Medlar taught us the value of the leucocytic picture as a whole as portraying the status of the lesion.

In Medlar's concept of the pathogenesis of tuberculosis[2] the monocyte is described as the cell forming the primary tubercle and also taking a large part in the repair of tuberculous lesions following caseation. The neutrophile is the chief cell in the formation of tuberculous abscesses. These may rupture and discharge leaving ulcers or cavities and so long as these ulcers or cavities continue to enlarge, the neutrophile continues to play a very prominent rôle. In the event the tuberculous abscess does not rupture but undergoes caseation and becomes walled off, the neutrophile ceases to play a significant part. The lymphocyte appears in the process as a predominant cell only when the lesion is in the healing stages. No definite rôle is ascribed to the eosinophile or basophile. The rôle each cell type plays in the tuberculous lesion is reflected in the peripheral blood. When neutrophiles are above 5,000 per cubic millimeter of blood, one may judge that tuberculous lesions are undergoing abscess formation or that ulcerous tuberculous lesions are becoming extended. When the monocytes are above 700 per cmm. of blood there is evidence of new tubercle formation. If the lymphocytes are above 2,000 per cmm., healing is in progress.

Other investigators have corroborated Medlar's work. However, there is still much skepticism as to the value of this test in judging activity in tuberculosis. Considering the fact that the white blood count is widely used in other infectious diseases, it is even more surprising that relatively little use is made of it in tuberculosis. The fact that in many instances we are dealing with the subacute and chronic stages of the disease may perhaps account to a certain extent for the lag in the application of this test. Marked elevations of the leucocyte counts are as a rule infrequent in the more chronic stages, and small to moderate elevations are apt to be glossed over as of no clinical significance. However, when a fairly large number of patients are tested it is found that the greatest majority show definite elevations of their total leucocyte counts and many of the counts are of the septic type. (In the septic leucocyte picture[2] the total count is usually above normal, at times it may be normal or even below normal, neutrophiles always above 65 per cent or usually 70 per cent or more; the lymphocytes never above 25 per cent, usually below 20 per cent; the monocytes are usually above 8 per cent, but they may be as low as 5 per cent.) Furthermore, the elevated counts and septic leucocyte pictures are by no means limited to the far-advanced clinically active cases, they are to be found in considerable numbers among the moderately advanced and even minimal cases. When patients are followed with frequent leucocyte counts, it is found that the septic leucocytic pictures persist as long as there are clinical indications for rest treatment or clinical signs of activity and in some instances even beyond that period. On the other hand when arrest of the disease is well-established, the leucocytic picture becomes non-septic.

The following table shows the relative frequency of elevated total counts and septic leucocytic pictures in a group of 356 patients with pulmonary tuberculosis. The series comprises 356 total and differential counts on 356 consecutive admissions to the Middlesex County Sanatorium. The entire series of cases was divided into five groups according to the classification of the National Tuberculosis Association. The incidence of positive sputum and elevation of temperature is given in each group.

It will be noticed that over 70 per cent of the entire series had total counts above the higher limit of normal (normal range from 6,000 to 9,000 cells per cmm. of blood) and the percentage of elevated counts increases as we proceed from the minimal to the very far-advanced groups, particularly the far-advanced B and C groups which contained the largest number of patients with both extensive and active disease (over 73 per cent of group C and over 26 per cent of group B were already dead at the time this report was written, that is, within two years of admission to the sanatorium. The percentage of deaths for group A was 3, and no deaths occurred among the moderately advanced and minimal cases). As would be expected, these groups showed the greatest numbers of elevated counts and the very high counts were practically limited to these groups. It should

*Read before the Section of Tuberculosis of the Massachusetts Medical Society, at its Annual Meeting, Worcester, June 6, 1934.

†Kaminsky, Jacob—Senior Physician, Middlesex County Sanatorium. For record and address of author see "This Week's Issue," page 285.

also be emphasized that the first three groups showed a considerable number of elevated counts. It will also be noticed that the percentage of septic leucocyte pictures increased rapidly as we proceed to the groups with increased activity and again attention is invited to the very considerable number of septic leucocyte pictures in the first three groups. It will also be seen that the percentage of septic leucocyte pictures far exceeds the percentage of resistance to the disease, and the blood picture will reflect this condition by a marked suppression of the lymphocytes, high percentage of neutrophiles and possibly an increase in the monocytes or a very low percentage of monocytes. Again, another patient with active and extensive disease may show marked clinical and x-ray improvement following institution of treatment. The leucocyte count in such instances may also show a marked change. There may be a drop

TABLE I

DATA FOR 356 ROUTINE ADMISSION BLOOD COUNTS IN A SERIES OF 356 CONSECUTIVE CASES OF PULMONARY TUBERCULOSIS

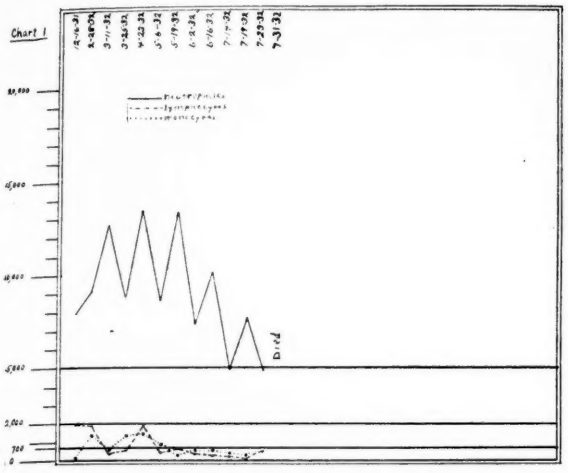
Classification on Admission (N.T.A.)	Number of Cases in Each Group	Positive Sputum	Temperature above 99°F.	Number of Total Counts Above 9,000	Number of Total Counts Above 12,000	Number of Total Counts Above 15,000	Number of Total Counts Above 18,000	Number of Septic Blood Pictures
Minimal	35	2 5.7%	6 17.1%	15 42.8%	1 2.8%	0 0%	0 0%	10 28.5%
Moderately Advanced	40	21 52.5%	12 30.0%	24 60.0%	8 20.0%	1 2.5%	0 0%	19 47.5%
Far Advanced—A	136	102 75.0%	42 30.8%	87 63.9%	36 26.4%	11 8.0%	2 1.4%	69 50.7%
Far Advanced—B	82	78 95.1%	67 81.7%	71 86.5%	43 52.4%	19 23.1%	6 7.3%	61 74.3%
Far Advanced—C	63	60 95.2%	58 92.0%	55 87.3%	36 57.1%	23 36.5%	16 25.3%	59 93.6%
Total	356	73.8% 263	51.9% 185	70.7% 252	34.8% 124	15.1% 54	6.7% 24	61.2% 218

counts above 12,000. This is a significant fact. It tends to show that many moderate or even slightly elevated blood counts are abnormal.

The above findings tend to illustrate in a general way the relationship between activity of the lesion and the leucocytic picture in pulmonary tuberculosis. This relationship may be observed even more specifically when patients are followed with repeated leucocyte counts. I have studied a group of tuberculous patients with frequent total and differential counts during the past two years. Over 1,200 total and differential counts were done. I have done over 1,100 of the differential counts myself and since, with few exceptions, the patients studied were under my immediate care, a good opportunity was afforded for correlating their blood trends with their clinical course.

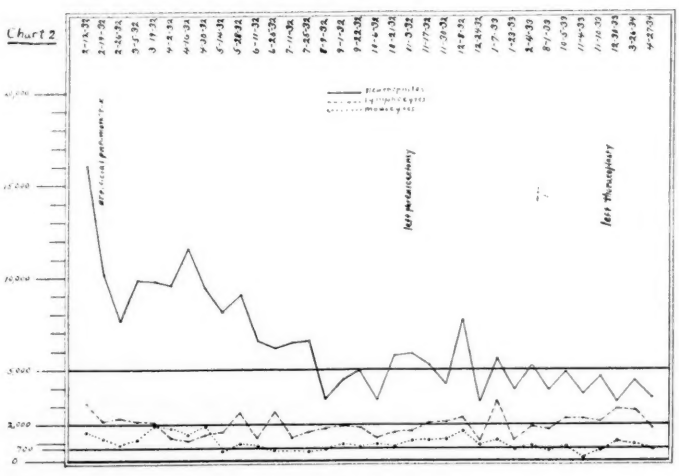
It was found that the leucocytic pictures may be in close agreement with clinical and x-ray findings throughout the course of observation in a given case. The patient may run an acute course with much toxemia, and no evidence of in the total count of 50 per cent or more denoting a decrease in the total volume of damaged tissue with the consequent lessened demand for cells of all types. The leucocyte picture, however, will continue to show a more or less septic trend until a definite stage of healing is reached. On the other hand, instances may be seen where the relationship between the leucocyte count and the clinical and x-ray findings is not very definite. However, it was found that when there is a discrepancy between the leucocyte count on one hand and the clinical and x-ray findings on the other, it is the clinical and x-ray findings which usually point to inactivity while the leucocyte picture is still of the septic type. Since experience has shown that patients who show exacerbations of their lesions have had septic blood pictures all along or their pictures have reverted to the septic type, it would seem justifiable to regard a septic blood picture as a sign of activity even if the clinical and x-ray findings still point in the other direction.

Three leucocytic graphs with brief clinical abstracts in each case will be presented to illustrate some of the above points.

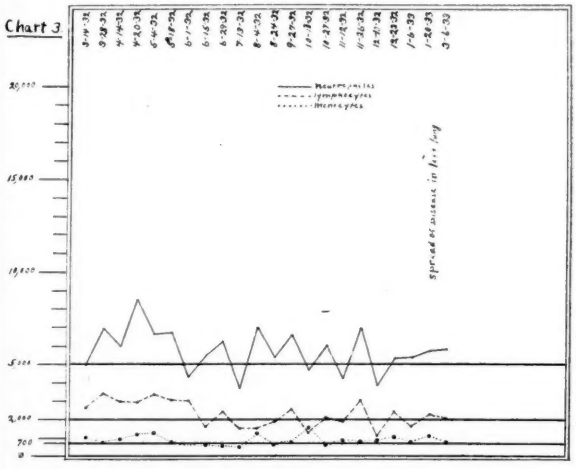


The first graph (chart 1) is that of a series of blood pictures in a far-advanced case with pulmonary tuberculosis (a woman, aged 27) who ran an active course with a fatal termination after nine months following her admission to the sanatorium. Unilateral pneumothorax was of no avail. The disease spread to the other lung. There were symptoms of intestinal tuberculosis. Autopsy revealed widespread tuberculosis in her lungs and the other organs including the intestines, liver, spleen, kidneys and uterus.

The leucocytic picture was of the septic type throughout. The neutrophiles were high ranging from 92 to 98 per cent in some counts. The monocytes were also elevated at first. The lymphocytes were low from the start and still further suppressed in later counts. The blood picture was in complete agreement with other findings in this case.



This graph (chart 2) is that of a series of blood pictures in another case of far-advanced active pulmonary tuberculosis (a man, aged 23) who, unlike the previous patient, responded markedly to bed rest and artificial pneumothorax. Attention is invited to the drop in the neutrophiles following institution of artificial pneumothorax. Frequent septic blood pictures, however, were still in evidence for some time and this was quite in agreement with clinical and x-ray findings. He continued to show a positive sputum till October, 1933 and there was evidence of uncollapsed cavities by x-ray examination. Left phrenicectomy was done November 2, 1932. Thoracoplasty was performed in November, 1933 and a second stage in December, 1933 with complete closure of cavities. Sputum has been negative since. The patient was discharged from the sanatorium in April, 1934 in excellent condition. A blood picture done shortly before operation and those done following the operation were definitely non-septic. This is another illustration of close agreement between the leucocytic picture and clinical and x-ray findings.



This graph (chart 3) is of a series of blood pictures in a far-advanced case of pulmonary tuberculosis (a woman, aged 28) who has apparently responded well to artificial pneumothorax treatment, but who after seventeen months of treatment had a flare-up in the con-

tralateral lung preceded by several hemoptyses. The right lung was well collapsed and there was but a small amount of productive infiltration in the left upper lobe which showed practically no change during the seventeen months of observation. The leucocyte count in this case revealed the true status of the lesion. It indicated activity, perhaps not of a high degree, but the septic trend of the blood picture was definite. Frequent elevations of the neutrophiles and monocytes continued in spite of an apparently effective pneumothorax and clinical improvement. This case illustrates the value of the leucocyte count in detecting the lower grades of activity which after all is most important since the higher grades of activity are, as a rule, accompanied by definite clinical signs.

REFERENCES

1 Cunningham, R. S., Sabin, F. R., Sugiyama, S., and Kindwall, J. A.: The rôle of the monocyte in tuberculosis. Bull. Johns Hopkins Hosp. 37:231, 1925.
2 Medlar, E. M.: An evaluation of the leucocytic reaction in the blood as found in cases of tuberculosis. Am. Rev. Tuberc. 20:312, 1929.

CHAIRMAN MORGAN. Our next paper will be "The Monocyte-Lymphocyte Ratio," by Dr. Gulli Lindh Muller, Rutland State Sanatorium.

THE MONOCYTE-LYMPHOCYTE RATIO AS A MEASUREMENT OF ACTIVITY IN PULMONARY TUBERCULOSIS*

BY GULLI LINDH MULLER, M.D.,† WITH THE TECHNICAL ASSISTANCE OF DORIS L. DAVIDSON†

IN a chronic disease like tuberculosis it is often difficult to determine the degree of activity in the pathological lesion demonstrated by x-ray and physical findings. This is especially true when the patient first seeks medical aid as sufficient time has not elapsed for controlled observations. At this time many questions have to be answered with regard to diagnosis, prognosis, and the length of time needed for treatment. It is also equally difficult to determine the degree of activity present after treatment has been instituted and the clinical signs and symptoms have subsided. Therefore, in 1925 when Cunningham and associates demonstrated with the supravital technique that in experimental[1] as well as clinical[2] tuberculosis, definite changes occur numerically in the monocytes and lymphocytes of the peripheral blood, this discovery was hailed as another criterion for determining the activity of a tuberculous process. From their work, Cunningham and his associates formulated a theory that the increase of the monocytes was an index of dissemination of the disease and the increase of the lymphocytes, an index of resistance. On the basis of that assumption they suggested that the ratio between the monocytes and the lymphocytes as expressed by the formula

$$\frac{\text{Total number (or percentage) of monocytes}}{\text{Total number (or percentage) of lymphocytes}}$$

would give in mathematical form an index of the relationship of the processes of tuberculous infection to those of resistance. They found that this monocyte-lymphocyte ratio was high when the disease was active, and normal or low when the patient had good combative powers. In their opinion the changes of the blood were so consistent in relation to the clinical changes that they felt it was equally possible to predict the clinical status from the blood findings or vice versa. The changes in the blood were therefore valuable from a prognostic and a diagnostic standpoint.

The work of Cunningham and associates has been verified by Blackfan and Diamond[3], Finner[4] and others using the supravital technique. The supravital technique, admirably adapted for the identification of young or modified cells is, however, too specialized and time consuming for clinical work, and therefore has not been used except for limited studies.

To determine whether the monocyte-lymphocyte ratio is of any real practical aid in evaluating activity in pulmonary tuberculosis, the blood counts of 800 consecutive admissions at the Rutland State Sanatorium have been analyzed. If a correlation could be demonstrated, in an unselected group of cases, between this ratio on admission and the clinical findings, it is felt that more practical information could be obtained than by studying a selected group of cases. The clinical data chosen were the stage of the disease, representing the extent of the lesion; the increase in pulse and temperature indicative of clinical activity; and the prognosis, reflecting indirectly the clinical judgment of the extent and the activity of the disease and the combative powers of the patient. In formulating the opinion about each individual patient, the monocyte-lymphocyte ratio was not considered. In addition the ratio on admission has been correlated with the subsequent results obtained for the purpose of determining whether it could be of aid in formulating prognosis.

*From the Rutland State Sanatorium, Rutland, Massachusetts.
Read before the Section of Tuberculosis of the Massachusetts Medical Society, at its Annual Meeting, Worcester, June 6, 1934.
†Muller, Gulli Lindh—Pathologist, Rutland State Sanatorium. Davidson, Doris L.—Laboratory Assistant, Rutland State Sanatorium. For records and addresses of authors see "This Week's Issue," page 285.

The counts were all made by one person on fixed cover slip smears, according to standard procedures. Many of them were checked by the author. That counts obtained from fixed smears compare favorably quantitatively with supravital counts has been shown by Morriss and Tan[5] and Blackfan and Diamond[3], an experience also verified by the author. In all determinations white blood cell counts were made, but in this paper no consideration has been given to the fact that the same numerical ratio may be obtained by widely varying total figures as well as percentages. Suffice it to say that the lower the percentage as well as total number of lymphocytes the graver the outlook for the patient, regardless of whether the monocytes increase, decrease or remain stationary. In addition to the admission counts on 800 patients, 300 cases have been followed over considerable periods of time. The results obtained in the latter group will be used only incidentally in this paper.

The normal average monocyte-lymphocyte ratio as found by various authors is about 0.3[2, 3, 6]. In table I the patients have been grouped according to the monocyte-lymphocyte ratio found on admission. Among the 800 consecutive admissions there were 730 cases of pulmonary tuberculosis, 13 cases of childhood type and, as a rule, inactive tuberculosis, 7 cases of pleurisy with effusion and 50 cases non-tuberculous.* The majority of the cases with childhood type of tuberculosis and those classified as non-tuberculous had a practically normal monocyte-lymphocyte ratio. Also correlating the only absolutely reliable finding for diagnosing tuberculosis, namely, the demonstration at some time of the tubercle bacillus either in sputum, body fluid or tissues obtained by biopsy or autopsy, the percentage of confirmed diagnoses increased in proportion to the monocyte-lymphocyte ratio to reach even 100 per cent in some of the groups with a high ratio. In pleurisy with effusion, especially in the acute stages, the ratio tended to be high.

In table II the monocyte-lymphocyte ratio of 730 patients with pulmonary tuberculosis has been correlated with various factors as the stage of the disease, prognosis, temperature and pulse during the first week after admission, and the results obtained during the time of observation.

Stage of the disease: In the group classified as minimal tuberculosis, or Stage I, the greatest number of cases had a normal or nearly normal ratio, and no patient was classified as Stage I with a ratio over 0.9. The cases classified as Stage II or moderately advanced, show the same trend as those of Stage I, while the percentage of far advanced cases or Stage III gradually increased with the ratio to a total of 94 per cent when this ratio reached 1.25 or over.

Prognosis: At the Rutland State Sanatorium the prognosis represents the consensus of the majority of the staff. A good prognosis indicates that the patient has practically a hundred per cent chance, a fair prognosis that there is an even or slightly better than even chance, a guarded prognosis that the patient has less than an even chance and a poor prognosis that the chance is practically nil. Comparing this clinical judgment with the objective finding of the monocyte-lymphocyte ratio, there was a surprisingly close correlation between these factors. The number of patients given a favorable prognosis decreased as the ratio increased and vice versa. In the group with a normal ratio the clinical judgment was apt to be somewhat pessimistic as was proved by subsequent results, while in the group with a high ratio the outcome was not always so unfavorable as would be indicated by the composition of the blood.

Temperature and Pulse: During the first week in the Sanatorium 18.9 per cent of the

TABLE I

THE MONOCYTE-LYMPHOCYTE RATIO IN RELATION TO DIAGNOSIS IN 800 ADMISSIONS

M:L Ratio	Number of Cases		Diagnosis				
	Total	%	Pulm. Tbc. %	Hilum Tbc. %	Pleurisy with Effusion %	Non Tbc. %	T.B. Found %
0.10—0.29	140	17.5	79.3	5.7	0.7	14.3	40.0
0.30—0.39	158	19.8	89.2	2.0		8.8	62.0
0.40—0.49	115	14.3	93.0	0.9		6.1	80.0
0.50—0.59	119	14.8	92.4	0.8	0.8	6.0	79.8
0.60—0.69	67	8.4	97.0		3.0		88.0
0.70—0.79	67	8.4	97.0		1.5	1.5	88.0
0.80—0.89	35	4.4	100.0				85.7
0.90—0.99	28	3.5	100.0				100.0
1.00—1.24	36	4.5	97.2			2.8	97.2
1.25 up	35	4.4	94.3		5.7		97.1

*In the latter group 32 were unclassified, 10 had bronchiectasis, 3 lung abscess, 3 new growth of the lung, 1 Hodgkin's disease, and 1 had pyopneumothorax, proved by autopsy to be non-tuberculous. The latter case had a monocyte-lymphocyte ratio over 1.0.

TABLE II

THE MONOCYTE-LYMPHOCYTE RATIO ON ADMISSION IN 730 CASES OF PULMONARY TUBERCULOSIS

M:L Ratio	No. of Cases Total	No. of Cases %	Stage of Disease I %	Stage of Disease II %	Stage of Disease III %	Prognosis Good %	Prognosis Fair %	Prognosis Guarded %	Prognosis Poor %	Signs of Activity 1st Week Temp. %	Signs of Activity 1st Week Pulse %	Results Imp. %	Results Unimp. %	Dead %	No. Data %
0.10 — 0.29	111	15.2	28.8	53.1	18.1	47.7	29.7	14.4	8.2	18.9	51.3	88.2	9.1	2.7	
0.30 — 0.39	141	19.3	21.3	48.9	29.8	41.1	31.9	12.7	14.1	33.3	67.3	78.7	14.3	5.6	1.4
0.40 — 0.49	107	14.7	11.2	44.8	43.9	28.0	32.8	21.4	17.8	41.1	67.2	72.9	17.7	8.5	0.9
0.50 — 0.59	110	15.0	3.6	49.1	47.3	20.0	29.1	21.8	29.1	50.9	77.2	61.8	21.8	13.7	2.7
0.60 — 0.69	65	8.9	3.1	41.5	55.4	23.0	23.0	17.0	37.0	55.3	76.9	44.6	27.6	23.1	4.7
0.70 — 0.79	65	8.9	7.6	46.2	46.2	16.9	30.7	32.4	20.0	60.0	81.5	55.3	21.6	20.0	3.1
0.80 — 0.89	35	4.8	2.8	25.7	71.5	11.4	17.2	31.4	40.0	71.4	88.5	42.8	20.0	37.2	
0.90 — 0.99	28	3.8		28.6	71.4	7.2	14.3	32.1	46.4	82.1	96.4	42.9	17.9	39.2	
1.00 — 1.24	35	4.8		11.4	88.6	2.9	20.0	22.8	54.3	91.4	94.2	20.0	25.8	51.4	2.8
1.25 up	33	4.6		6.0	94.0	3.0	9.1	21.2	66.7	78.7	93.9	27.2	15.2	51.5	6.1

patients had elevated temperature and 51.3 per cent increased pulse rate in the group with normal monocyte-lymphocyte ratio. The percentage of patients with elevated temperature and pulse rate above normal increased progressively with the ratio but did not reach 100 per cent in any one group.

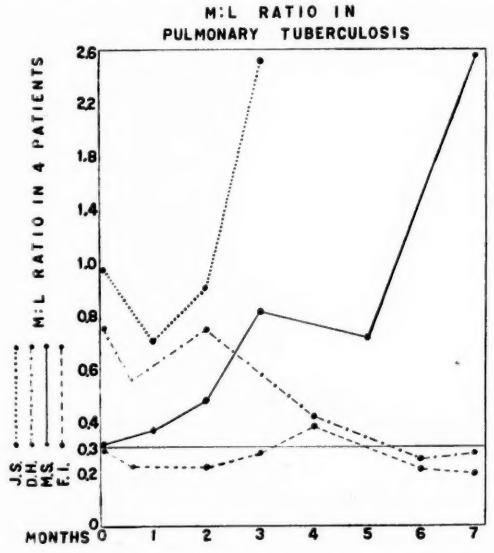
Results obtained during the time of observation: Under the heading "improved", quiescent and arrested cases have been included, and under "unimproved" those that were stationary or failing.

In the group of 111 patients with a normal monocyte-lymphocyte ratio 88.2 per cent improved. As the percentage of improving cases decreased the monocyte-lymphocyte ratio increased. It also increased proportionally to the increasing number of unimproved or dead cases. The unfavorable results in the group with a normal ratio seem more apparent than real, from the point of view of tuberculosis. Three patients or 2.7 per cent died. None of the deaths was directly attributable to the activity of pulmonary tuberculosis. One died from spontaneous pneumothorax following pneumolysis, one 19 months after admission from rheumatic heart disease of several years' duration, complicated by ulcerative endocarditis, and one 11 months after admission from subacute nephritis. Of the 10 cases or 9.1 per cent classified as unimproved one had typical bronchial asthma but was considered to have tuberculosis from x-ray findings. Four remained in the hospital a short time only, and 3 of these were over 60 years of age and had had tuberculosis for a long time. Four cases had had sanatorium treatment for from two and a half to three and a half years before admission, all of them being stationary, and 3 of them now waiting for thoracoplasty.

That a considerable number of patients with tuberculosis will have a normal monocyte-lymphocyte ratio is illustrated in chart I. The ratio of 4 patients obtained during their stay in the hospital has been charted. Two of them had a normal ratio at some time while one, (F. I. 18028) a minimal case without symptoms diagnosed by the tuberculin reaction and x-ray in a routine school examination, had a normal ratio throughout. In the second case (D. H. 18032) the disease was moderately active and the monocyte-lymphocyte ratio moderately high on admission, but the patient improved rapidly under collapse therapy and the ratio came down to normal. In a third patient (M. S. 18041) classified as Stage II with a fair prognosis the monocyte-lymphocyte ratio on admission was 0.7. She improved steadily for about 22 months and the ratio came down to normal. Then she developed a bronchopleural fistula with marked reactivation of symptoms. The course of the disease, during the last 7 months of life corresponded to the rise in the ratio, which shortly

before the fatal outcome reached 2.55. (See chart.) The fourth case (J. S. 18414) was terminal on admission.

In the group with a monocyte-lymphocyte ratio of 1.0 or over, 16 improved. This indicates that a pessimistic view as to the outcome in the presence of a high ratio is not always justifiable, although, from the results obtained, a high ratio must be considered with grave concern.



F. I. (18028) Stage I. Prognosis good. No symptoms. Discovered at a routine school examination. Discharged with pneumothorax.
M. S. (18041) Stage II. Prognosis fair. M. L .ratio on admission two and a half years ago 0.7. Doing well until 7 months ago. Dead.
D. H. (18032) Stage III. Prognosis fair. Improved with collapse therapy.
J. S. (18119) Stage III. Prognosis poor. Dead.

A high ratio may be accounted for by various factors, the nature of which must be carefully studied in order to avoid misleading interpretation. Into this category enters an acute onset with a cold, bronchopneumonia, pneumonia or pleurisy. Successful active therapy may also bring about a rapid change in the monocyte-lymphocyte ratio. However, 25 per cent of the patients with a ratio over 1.0 were dead within 3 months. The results obtained in the various groups and the time of observation are recorded in table III. From the examination of the various tables it is seen that between the groups with normal and high ratios all stages of activity were represented.

SUMMARY AND CONCLUSION: From the analysis of the above data, obtained in most cases before the disease had been influenced by therapy, it is evident that practically every conceivable stage of pulmonary tuberculosis has been included. The ratios of the 730 patients on admission represent the various ratios that would be obtained in one individual patient during the whole course of his disease. At some time or other a patient with pulmonary tuberculosis will have a normal ratio, and the numerical ratio cannot therefore be used as a criterion in diagnosis.

In the group with normal or nearly normal ratio many were definitely active as indicated by the increase in pulse and temperature and other toxic phenomena. In addition many of these patients with a normal ratio showed an increase in the sedimentation rate and a shift to the left in the polymorphonuclear differential. The monocyte-lymphocyte ratio therefore is not a sensitive index of activity in the tuberculous patient.

However, even if the monocyte-lymphocyte ratio cannot be used as a diagnostic sign or as a reliable index of activity in tuberculosis, it furnishes a most valuable indication as to the manner in which an individual is handling his infection. In other words, it is a delicate, easily obtained test for measuring the resistance of the host to the invader. When the monocyte-lymphocyte ratio approaches normal, or reaches values below normal, there is a balance between the host and the invader in favor of the former, as demonstrated by the data in this paper. An increasing ratio, on the other hand, indicates that the host was waging a losing fight

TABLE III

THE MONOCYTE-LYMPHOCYTE RATIO OF 730 CASES OF PULMONARY TUBERCULOSIS ON ADMISSION IN RELATION TO THE RESULTS OBTAINED DURING THE TIME OF OBSERVATION

		Time of Observation									
		1 to 3 Months				3 to 6 Months			6 to 24 Months		
M:L Ratio	No. of Cases	Imp. %	Unimp. %	Dead %	No Data %	Imp. %	Unimp. %	Dead %	Imp. %	Unimp. %	Dead %
0.10—0.29	111	18.0	2.7			10.8	1.8		59.5	4.5	2.7
0.30—0.39	141	12.0	4.2	1.4	1.4	17.0	0.7	2.2	49.6	9.3	2.2
0.40—0.49	107	11.3	5.7	0.9	0.9	19.7	2.8	2.8	42.0	9.3	4.6
0.50—0.59	110	6.4	3.6	3.6	2.7	11.8	4.5	2.7	43.7	13.7	7.3
0.60—0.69	65	1.5	6.2	9.3	4.6	9.2	4.6	4.6	33.8	16.9	9.3
0.70—0.79	65	4.6	4.6	6.2	3.1	13.8	4.6	9.2	36.9	12.4	4.6
0.80—0.89	35	8.6	2.9	20.0		5.7		5.7	28.5	17.2	11.4
0.90—0.99	28	7.2		17.8		3.7		7.2	32.1	17.8	14.2
1.00—1.24	35	5.7	14.2	25.7	2.8	2.8	2.8	11.5	11.5	8.7	14.3
1.25 up	33			27.2	6.0	12.2	9.1	15.2	15.2	6.0	9.1

at the time the determination was made. It is clear that this is of great value in formulating prognosis.

It is also self-evident that repeated determinations of the monocyte-lymphocyte ratio are valuable in analyzing the patient's reaction to the infection and therefore serve as an aid in evaluating various forms of treatment. The monocyte-lymphocyte ratio, together with other information that can be obtained from the examination and correct interpretation of the blood, is an objective fact that can be substituted for personal opinion and it ought to be used more extensively than it is at present.

I am greatly indebted to Daniel A. Robinson for the preparation of the chart and tables, and to Miss Ethel M. Reese for assistance in preparing the manuscript.

REFERENCES

1 Cunningham, R. S., Sabin, F. R., Sugiyama, S., and Kindwall, J. A.: The rôle of the monocyte in tuberculosis. Bull. Johns Hopkins Hosp. 37:231, 1925.

2 Cunningham, R. S., and Tompkins, E. H.: The white blood cells in human tuberculosis. Am. Rev. Tuberc. 17:204, 1928.

3 Blackfan, K. D., and Diamond, L. K.: The diagnostic and prognostic significance of the white blood cells in active tuberculosis. South. M. J. 22:248, 1929.

4 Finner, L. L.: The clinical value of the monocyte count in pulmonary tuberculosis. Am. Rev. Tuberc. 21:764, 1930.

5 Morriss, W. H., and Tan, S. H.: The differential leucocyte count in pulmonary tuberculosis. The value of the lymphocyte-monocyte ratio in the determination of activity. Am. Rev. Tuberc. 16:729, 1927.

6 Medlar, E. M.: The extent of the variation in the leukocytes of normal individuals. Am. J. M. Sc. 177:72, 1929.

CHAIRMAN MORGAN: The next paper is "The Schilling Differential Count and Red Cell Sedimentation Rate," by Dr. John W. Cass, Jr., The Channing Home, Boston.

DR. JOHN W. CASS, JR.: *Mr. Chairman, Ladies and Gentlemen of the Section*—We consider this whole situation so vital that we have gone into some detail, taking into consideration the entire blood picture, as well as the sedimentation rate, and correlating these findings with the x-ray and clinical findings. I can just touch upon the high spots of our work, first, as distinguishing between clinical and pathological activity.

THE SCHILLING DIFFERENTIAL COUNT AND RED CELL SEDIMENTATION RATE AS A MEASUREMENT OF ACTIVITY IN PULMONARY TUBERCULOSIS*

BY JOHN W. CASS, JR., M.D.,† WITH THE TECHNICAL ASSISTANCE OF MARGARET SUTERMEISTER, B.S.†

ACTIVITY

THE activity of a disease is of two types, clinical and pathological. Clinical activity is expressed by the temperature, pulse, and the various other objective signs of infection and toxicity. These, however, are dependent upon the pathological state or pathological activity. The clinical state is not necessarily directly proportionate to the degree of pathological activity and thus one cannot be judged by the other. Duffy[1] clearly expresses the situation by stating, "The spread and progression of the lesion constitute pathological activity which, depending primarily on the allergic state prevailing at the time and secondarily on the two anatomical factors of location and character of the lesion, may go on to clinical activity." Pathological activity is, then, the representation of the allergic response influenced by the anatomical location of the lesion; and clinical activity, as typified by the usual objective criteria, is a portrayal of a pathological activity no longer latent.

The manifestations of clinical activity are, in most part, commonly known. However, it is apparent that, in tuberculosis, clinical activity is very often absent and thus it is important to demonstrate the presence or absence of pathological activity. The procedures used to demonstrate this state are many. The sedimentation rate, the total blood picture, the various groupings of the blood cells, the diazo-reaction, the Vermes test, the Daranye reaction, the Matefy reaction, and the phosphatid precipitant reaction, are some of the procedures in use at the present time. In this paper we are particularly interested in the sedimentation rate and the immature neutrophile cells as an index of pathological activity in tuberculosis.

SEDIMENTATION RATE

The fact that the red cells settle rapidly in the blood taken from an ill person has been known since the time of Hippocrates, and John Hunter makes mention of this phenomenon in his book, "Blood, Inflammation and Gunshot Wounds," published in 1797. However, the phenomenon seems to have been neglected until Robin Fahraeus[2] published his observations in 1918, and shortly afterwards, Linzenmeier[3] applied it to the study of pelvic inflammation.

There are many explanations offered for the increased rate of settling of the red cells, none of which are universally accepted. Auto-agglutination, electrophysical reaction, increased fibrinogen content of the blood plasma and a specific ferment in the plasma are some of the more common theories advanced. The more or less accepted facts are that the sedimentation rate depends on cellular destruction and that the rapidity of the rate is directly proportionate to the amount of cellular destruction. That is,

*Read before the Section of Tuberculosis of the Massachusetts Medical Society, at its Annual Meeting, Worcester, June 6, 1934.

†Cass, John W., Jr.—Physician, Channing Home. Sutermeister, Margaret—Formerly Research Assistant at University of Minnesota and Yale University. For records and addresses of authors see "This Week's Issue," page 285.

the sedimentation rate increases in all cases of increased protein catabolism. This includes any febrile condition, infection, disintegrating tumor, pregnancy, foreign protein reaction, advanced renal, and liver disease, during x-ray therapy, anemia, hyperthyroidism, and possibly advanced arteriosclerosis and the major psychoses; the explanation being that these conditions, by tissue destruction, alter the colloidal lability of the blood in such a way that the red blood cells settle out quickly from the plasma. It is now fairly clear that the sedimentation rate increases with a decrease in the total number of red blood cells and also perhaps that there is a significant relationship between the fibrinogen content of the plasma and the sedimentation rate. Greisheimer[4] and his fellow workers demonstrated that the sedimentation rate is independent of the total number of white blood cells, polymorphonuclear neutrophiles, and lymphocytes but is increased as the total number of red cells decrease and increased also as the fibrinogen content of the plasma increased.

The sedimentation time consists of three phases: first, a period of slow settling of the cells; secondly, a period of rapid settling; and thirdly, a period of packing of the red cells. The time lapsing before the period of packing represents the true sedimentation time. The sedimentation rate is the speed of settling of the red cells during the sedimentation time and has been represented in so many different terms by so many methods that the entire terminology is now extremely confusing.

The two common methods of determining the sedimentation rate are those introduced by Cutler[5] and by Rourke and Ernstene[6], the only essential difference being that Rourke and Ernstene corrected their results for the hematocrit and this seems to be a proper procedure. The charts devised by Cutler make a very satisfactory portrayal of the sedimentation rate and the test is accurate in the absence of anemia. There is some disagreement about the influence of the various anticoagulants on the sedimentation rate, heparin, oxalate, and citrate, in the order named, causing the least disturbance. As heparin is expensive and difficult to keep, the Rourke and Ernstene[6] procedure, using oxalate instead of heparin, seems to be the most satisfactory method at the present time.

The sedimentation rate is only specific of cellular destruction. It is not diagnostic of any particular disease but is a gauge of pathological activity in any disease. In regard to tuberculosis it is safe to say that a normal sedimentation rate is practically never found in a clinically active case. In this disease the test has been used extensively and by a great many workers, but their results and opinions cannot be covered in this paper. R. R. Trail[7] followed five hundred cases over a period of two to six years and found that, irrespective of their clinical state at the time of discharge, the majority of those who had a rapid sedimentation rate at the time of discharge ultimately did poorly. One certainly has the right to agree with the common belief of those who have used this procedure in the study of tuberculosis, that it is of distinct value as a gauge of activity, particularly in those cases apparently clinically inactive. What constitutes the normal sedimentation rate cannot be stated specifically at the present time without specifying the method used, but there is a definite tendency universally to use a method similar to that of Rourke and Ernstene[6] and the present confusion is slowly clearing. Possibly before this standardization is reached, a method taking into consideration the fibrinogen content of the blood, as well as the hematocrit, will have to be devised.

THE SCHILLING DIFFERENTIAL COUNT

That the blood constituents change during clinical activity of a disease has been known for many years. Cunningham, Sabin[8], and their workers demonstrated in experimental tuberculosis that cellular changes in the peripheral blood during the course of the disease were related to the activity. Medlar[11] and Schilling[9] demonstrated the importance of the classification of the different types of cells as an index of activity. Schilling's[9] classification of neutrophiles constitutes our interest in this paper. His mature polymorphonuclears contain nuclei with two or more segments, the immature polymorphonuclears a single nucleus, and he further differentiates the immature cells into juveniles and stab or band cells. The juveniles, or very young cells, he describes as large with kidney or sausage-shaped nuclei, rich in chromatin, rather faintly stained, clouded with prominent nuclear elements, and having nucleoli at the bulbous ends of the nuclei, the cytoplasm being the same as in the adult neutrophiles. The older stab or band cells he describes as having a thinner nucleus which is s-, u-, or v-shaped, with dense, heavy chromatin elements and no nucleoli. It is stated by Schilling[9] that the stab or band cells increase first in infection and, if above three to five per cent in the peripheral blood, a toxic element is considered to be present which is retarding the normal development of the myelocytes and juveniles into mature neutrophiles. He terms such a picture a degenerative blood with a shift to the left of the neutrophile leucocytes. This term "shift to the left" was originally used by Arneth[10], meaning an increase in neutrophiles with unsegmented nuclei at the expense of segmented or mature forms. Schilling[9] further maintains that in a more severe state of toxicity or infection, the bone marrow is overstimulated, the myelocytes develop more rapidly, and immature juvenile types are poured into the circulation

before they reach the stab or band stage. This state he calls a regenerative picture.

The terms "degenerative" and "regenerative" are confusing if we wish to apply them to a clinical state of mild or severe infection but they are clear as used to depict a blood condition. A further stage than the regenerative picture, following this line of reasoning, would be the presence of myelocytes and, finally, the extreme state of complete inhibition or absence of neutrophiles in the peripheral circulation.

Schilling's[9] "shift to the left", then, as with Arneth[10], means an increase of unsegmented neutrophiles which may be degenerative, as typified by an increase of the stab or band cells, or regenerative with an increase of the juvenile cells. His normal hematogram is as follows:

Basophiles	0— 1%
Eosinophiles	2— 4%
Myelocytes	0
Juveniles	0
Stab or band cells	3— 5%
Segmented cells	58—66%
Lymphocytes	21—25%
Monocytes	4— 8%

Duffy[1], in studying tuberculosis, found that a shift to the left or an increase in the unsegmented cells usually preceded trouble and that the finding was most constant in the minimal cases and more consistent in general with the x-ray picture than the clinical picture. Most of the information available appears in agreement that a shift to the left is present in clinically active tuberculosis and that it is reasonable to expect that this shifting should occur before and after evidence of clinical activity. In tuberculosis, the increase of the immature cells is usually of the stab or band variety but there may be an increase of the juveniles in a severe infection. Medlar[11] reasoned that, as the cytological changes are among the first pathological occurrences in disease, variations in the constituents of the peripheral blood should precede x-ray and clinical manifestations and so it seems reasonable that the Schilling differential count can be used as an indicator of pathological activity in tuberculosis. The count can also be used in conjunction with tuberculin injections as an indicator of activity and there are considerable data in the literature on the value of this procedure.

It is dangerous to try to merge from using this procedure as an indicator of activity to its use as an indicator of prognosis for, although the blood can measure activity as well as favorable reactions toward healing, prognosis is related to a great many mechanical and unforeseen factors, such as sudden rupture of a tuberculous abscess, sudden complications of meningitis, pneumonia, massive hemoptysis, and cardiac failure. As with the sedimentation rate, this differential count cannot be considered a diagnostic procedure, but we believe it does indicate the presence of pathological activity.

DATA FROM THE CHANNING HOME CASES

The following data were obtained from a study of thirty-five female patients, ranging in age from seventeen to fifty-three years. The same technician performed the laboratory work. The same clinician followed the cases and did the check-up examinations. The white blood counts, blood smears, and blood sedimentation rates were repeated on each patient at approximately two-week intervals. The white blood counts and the blood smears for the Schilling counts were taken simultaneously. The standard methods of blood counting technique were followed and for the Schilling, 200 cells were counted on smears on cover slips, stained by the Wright method. In differentiating the young and mature polys, a mature or segmented form was considered to be any cell which had a nucleus of two or more lobes separated by a thread. As the nucleus became more unified and the thread-like junction became wider, it was termed a stab or band cell. When the cell appeared to contain a nucleolus, it was termed a juvenile form.

In determining the red cell sedimentation rate the method employed by Rourke and Ernstene[6] was used, the fastest even rate of settling was determined, the result being expressed in millimeters per minute. Heparin was used as the anti-coagulant. The hematocrit of each specimen was determined and the sedimentation rate corrected for variation from the normal by means of the special chart constructed by Rourke and Ernstene[6]. The normal limits of the corrected sedimentation rate were considered from 0.08 to 0.4 mm. per minute. The highest sedimentation rates and the greatest number of immature polymorphonuclear neutrophiles were found in the most active clinical cases and in all cases, the blood findings fairly closely paralleled the clinical state. In the cases not clinically active but of proved diagnosis, the blood findings were above normal.

The check-up examination consisted of a brief history, the patient's weight, physical examination of the chest, x-ray examination of the chest in all but four cases, and the sedimentation rate, the total white blood count, routine differential count, including Schilling differential count and also the Medlar classification.

The thirty-five cases were subdivided as ten minimal, eleven moderately advanced, and ten far advanced, according to the customary classification. The remaining four were classed as very far advanced or apparently hopeless. All ten minimal cases were clinically inactive throughout their stay in the Home and the diagnosis was made on the history and x-ray findings of questionable activity. The sedimentation rates, Schilling counts, and the entire blood pictures of these cases were above normal through-

out their stay of three to twelve months. However, they all showed definite improvement at the time of discharge. On check-up, three to fifteen months following discharge, nine were still clinically inactive and their blood was either the same as on discharge or improved. The tenth case was found to have active tuberculous glands of the neck and the blood findings were moderately elevated.

All eleven moderately advanced cases were both clinically and pathologically active on admission with blood values well above the normal. All these cases were clinically inactive at discharge seven to seventeen months after admission. The blood in each case, however, was still above normal and in five cases, it had not improved. At check-up, three to fifteen months following discharge, all were clinically inactive, all had blood findings above normal, but seven cases had improved blood findings. Three of this group had pneumothorax therapy and three had evulsion of the phrenic nerve.

All ten far-advanced cases were clinically active on admission, with the complete blood, Schilling and sedimentation rate, markedly elevated. Four of these cases had been discharged three to nineteen months following admission, clinically inactive, with active but improved bloods. Six cases are still in the Home ten to twenty-five months after admission, clinically active and with very active bloods. A check-up of the four discharged cases two to twelve months after they had left the Home showed them to be clinically inactive with improved but still active blood findings. Of these far-advanced cases, four had pneumothorax therapy, two being bilateral cases; four had thoracoplasty with phrenic evulsion; and two had phrenic evulsion alone.

Of the four very far-advanced cases, three died within three to eight months after admission with greatly elevated blood findings. One was discharged three and one-half years following admission, clinically inactive but with moderately elevated blood findings. On check-up twelve months after discharge, this patient was still clinically inactive and still had elevated blood findings which were, however, definitely improved over the findings at the time of discharge.

The following tables are included to present as adequately as possible the status of the patients at the time of admission, discharge, and check-up examinations. The laboratory data on admission are the average for the first month, that on discharge the average for the last month, and on the check-up examination only one blood study was obtained.

SUMMARY AND CONCLUSION

We do not attempt to draw any definite conclusions from our small series but we have found by doing frequent sedimentation rates, Schilling counts, and total white blood counts with the Medlar and the usual differential count, that, in spite of the occasional disagreement among the findings over a period of time, a curve is obtained of the pathological state which fairly well parallels the clinical status of the patient. We found also that this curve continues on in a declining fashion after all evidence of clinical activity has ceased.

It is difficult to select one procedure as the ideal indicator of pathological activity. The sedimentation rate plus the entire cellular blood picture appears to go together and only as a whole to give the proper information. Personally, I feel that frequent, properly performed sedimentation rates would probably give adequate portrayal of the pathological state of the patient. In the cases followed longest, the immature polys have been slightly above normal, even when the sedimentation rate and the total white blood count picture has returned to normal. The blood findings at approximately two-week intervals with our cases have not been of value in prognosticating trouble but have rather changed about the same time or soon after a clinical upset. A temporary increase in the sedimentation rate has been noted following the beginning of pneumothorax treatment. There has been a gradual improvement in the entire blood picture following this rise, dependent on the success of the collapse.

It is, of course, not practical to go on the assumption that a patient long clinically inactive with inactive x-ray can be kept in a sanatorium or even on a semi-invalid routine until the blood returns absolutely to what we now consider normal values. The entire blood curve must be taken into consideration in deciding this point. It does seem safe to say, however, that a person clinically inactive but with blood values considerably above normal must be handled with great caution. In every case of tuberculosis the question at some time arises as to the state of activity and the wisdom of attempting to start the patient on return to a normal program. This decision is usually made on the basis of the clinical course and the serial x-ray picture. This is only a rough guess influenced by the experience of the physician as to the pathological state. As a part of the entire clinical status, a serial blood picture is indicated as an aid in deciding how to manage the tuberculous patient clinically inactive. The sedimentation rate and the Schilling count, as parts of the complete blood picture, are certainly worth while adjuncts to the x-ray and the clinical indicators of activity.

From the point of view of diagnosis, these procedures are also of great value. Just as the pathological state exists long after clinical quiescence, so it appears long before clinical activity manifests itself. All our minimal cases were clinically inactive and with indefinite

GROUP I—*Minimal Cases*

	Admission	Discharge	Check-Up
E. A.	12 months	3 months	
Aged 27	Sed. R. 0.5	0.5	0.8
	WBC 10,000	11,000	9,000
	B 27; Py 65	16 -60	25 -62
	Clinically inactive	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No change
D. C.	12 months	9 months	
Aged 24	Sed. R. 0.3	0.2	0.3
	WBC 7,000	7,000	7,000
	B 16;T Py 55;L 33;M 10	16 -64 -29 -3	12 -61 -31 -7
	Clinically inactive	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No change
D. C.	4 months	4 months	
Aged 30	Sed. R. 0.4	0.25	0.8
	WBC 8,000	6,000	9,000
	B 8;T Py 62;L 28;M 9	10 -57 -31 -11	14 -57 -33 -9
	Clinically inactive	Clinically inactive	Active glands
	X-ray ?active	No change	No x-ray
N. H.	5 months	11 months	
Aged 23	Sed. R. 1.1	0.6	0.65
	WBC 13,000	10,000	12,000
	B 13;T Py 72;L 17;M 6	9 -70 -22 -4	19 -68 -26 -6
	Clinically inactive	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No change
C. H.	7 months	10 months	
Aged 21	Sed. R. 0.7	0.5	—
	WBC 11,000	10,000	—
	B 24;T Py 69;L 25;M 4	13 -68 -26 -4	—
	Clinically ?active	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No x-ray
H. L.	4 months	9 months	
Aged 35	Sed. R. 1.0	0.6	0.6
	WBC 6,000	6,000	6,000
	B 27;T Py 54;L 35;M 10	19 -47 -40 -11	16 -56 -32 -9
	Clinically, pleurisy	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No change
S. M.	8 months	13 months	
Aged 22	Sed. R. 0.6	0.3	0.9
	WBC 10,000	11,000	10,000
	B 14;T Py 70;L 20;M 7	21 -66 -23 -8	25 -74 -18 -7
	Clinically ?active	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No change
R. M.	4 months	15 months	
Aged 53	Sed. R. 0.9	0.6	0.65
	WBC 11,000	9,000	10,000
	B 20;T Py 55;L 33;M 6	17 -58 -28 -8	16 -58 -29 -8
	Clinically inactive	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No x-ray
E. S.	6 months	10 months	
Aged 18	Sed. R. 0.4	0.4	0.4
	WBC 9,000	11,000	10,000
	B 11;T Py 71;L 19;M 8	9 -67 -23 -7	6 -72 -22 -5
	Clinically inactive	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No change
A. W.	7 months	14 months	
Aged 33	Sed. R. 0.6	0.7	0.7
	WBC 8,000	9,000	8,000
	B 20; T Py 71;L 24;M 4	22 -62 -25 -12	21 -66 -28 -6
	Clinically inactive	Clinically inactive	Clinically inactive
	X-ray ?active	No change	No change

GROUP II—*Moderately Advanced Cases*

	Admission	Discharge	Check-Up
G. C.	11 months	3 months	
Aged 34	Sed. R. 1.3	0.5	0.55
	WBC 11,000	11,000	11,000
	B 10;T Py 72;L 22;M 5	5 -70 -25 -3	5 -69 -24 -5
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	X-ray inactive
G. C.	13 months	4 months	
Aged 38	Sed. R. 0.8	0.3	0.3
Pneumothorax	WBC 13,000	10,000	11,000
	B 32;T Py 73;L 25;M 8	16 -61 -28 -5	11 -57 -33 -5
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	No change
N. C.	15 months	5 months	
Aged 20	Sed. R. 1.3	1.2	0.5
Pneumothorax	WBC 16,000	16,000	15,000
	B 12;T Py 75;L 18;M 6	25 -73 -16 -8	22 -70 -16 -11
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	No change
M. D.	10 months	11 months	
Aged 43	Sed. R. 0.9	0.8	0.7
Phrenic	WBC 10,000	9,000	11,000
	B 5;T Py 54;L 31;M 9	6 -59 -31 -6	5 -46 -41 -5
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	No change
L. F.	17 months	15 months	
Aged 39	Sed. R. 1.0	1.0	0.5
Phrenic	WBC 9,000	8,000	10,000
	B 15; T Py 74;L 18;M 5	10 -70 -15 -12	22 -77 -15 -6
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	No change
H. G.	14 months	3 months	
Aged 29	Sed. R. 1.4	0.9	1.1
Pneumothorax	WBC 13,000	13,000	11,000
	B 13;Py 63;L 28;M 9	6 -63 -31 -5	3 -64 -29 -5
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	No change
L. R.	12 months	11 months	
Aged 18	Sed. R. 1.0	0.8	0.8
Phrenic	WBC 15,000	17,000	14,000
	B 10;T Py 54;L 36;M 8	21 -65 -25 -7	14 -64 -26 -6
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?active	No change
E. S.	13 months	8 months	
Aged 27	Sed. R. 0.5	0.4	—
	WBC 12,000	12,000	—
	B 8;T Py 64;L 27;M 5	10 -67 -24 -7	—
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	X-ray inactive
D. W.	12 months	3 months	
Aged 29	Sed. R. 1.0	0.4	0.4
	WBC 14,000	14,000	12,000
	B 20;T Py 72;L 17;M 8	13 -70 -22 -6	13 -72 -17 -8
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	No change
P. H.	13 months	12 months	
Aged 24	Sed. R. 1.0	0.4	0.45
	WBC 13,000	8,000	9,000
	B 36; T Py 63;L 25;M 9	19 -59 -30 -7	23 -69 -20 -9
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	X-ray inactive
M. C.	7 months	3 months	
Aged 43	Sed. R. 0.6	0.5	0.65
	WBC 11,000	9,000	14,000
	B 13;T Py 43;L 46;M 5	11 -48 -41 -4	12 -50 -40 -6
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?active	No change

GROUP III—*Far-Advanced Cases*

	Admission	Discharge	Check-Up
R. B.	3 months	12 months	
Aged 27	Sed. R. 1.1	1.2	0.8
Pneumothorax	WBC 21,000	21,000	13,000
	B 35;T Py 72;L 15;M 8	31 -67 -25 -7	11 -48 -44 -7
	Clinically active	Clinically active	Inactive
	X-ray active	X-ray active	?Inactive
*A. W.	18 months		
Aged 23	Sed. R. 1.2	0.5	
Pneumothorax	WBC 13,000	9,000	
	B 31;T Py 74;L 16;M 10	10 -44 -44 -7	
	Clinically active	Clinically inactive	
	X-ray active	?X-ray inactive	
*H.M.	10 months		
Aged 28	Sed. R. 1.1	1.4	
Phrenic	WBC 21,000	15,000	
	B 52;T Py 79;L 15;M 5 J 1.0	24 -60 -29 -11	
	Clinically active	?Clinically active	
	X-ray active	X-ray active	
*P. H.	18 months		
Aged 18	Sed. R. 1.6	1.1	
Thoracoplasty	WBC 17,000	13,000	
	B 19;T Py 74;L 18;M 8	12 -51 -42 -7	
	Clinically active	Clinically inactive	
	X-ray active	?X-ray inactive	
*M. McC.	18 months		
Aged 34	Sed. R. 2.0	0.8	
Thoracoplasty	WBC 12,000	8,000	
	B 19;T Py 64;L 24;M 12	9 -64 -26 -10	
	Clinically active	Clinically inactive	
	X-ray active	?X-ray inactive	
*A. C.	24 months		
Aged 22	Sed. R. 1.6	0.75	
Pneumothorax	WBC 10,000	10,000	
	B 21;T Py 67;L 22;M 8	12 -63 -28 -6	
	Clinically active	Clinically active	
	X-ray active	?X-ray inactive	
*L. L.	25 months		
Aged 40	Sed. R. 1.3	0.5	
Phrenic	WBC 14,000	12,000	
	B 26;T Py 81;L 9;M 8	23 -60 -25 -7	
	Clinically active	Clinically inactive	
	X-ray active	?X-ray inactive	
H. W.	19 months	12 months	
Aged 39	Sed. R. 0.8	0.5	0.35
Thoracoplasty	WBC 12,000	10,000	7,000
	B 11;T Py 68;L 24;M 6	8 -67 -25 -6	9 -63 -29 -6
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	?X-ray inactive	No change
H. M.	9 months	2 months	
Aged 28	Sed. R. 1.6	0.6	0.45
Thoracoplasty	WBC 13,000	13,000	11,000
	B 47;T Py 65;L 24;M 9 J. 0.5	38 -70 -18 -6	27 -59 -29 -7
	Clinically active	Clinically active	?Clinically active
	X-ray active	X-ray active	X-ray active
I. K.	8 months	10 months	
Aged 34	Sed. R. 2.0	1.6	0.95
Pneumothorax	WBC 16,000	16,000	9,000
	B 42;T Py 73;L 18;M 8	38 -65 -21 -9	26 -58 -29 -9
	Clinically active	Clinically active	?Clinically active
	?X-ray active	?X-ray active	

*Patients at present in Channing Home.

GROUP IV—*Apparently Hopeless*

	Admission	Discharge	Check-Up
M. H.	8 months		
Aged 21	Sed. R. 1.7	1.6	
	WBC 19,000	18,000	
	B 57;T Py 90;L 4;M 6	51 -78 -14 -8	
	J. 1		
	Clinically active	Died	
	X-ray active		
E. C.	6 months		
Aged 22	Sed. R. 1.9	1.6	
	WBC 17,000	16,000	
	B 60;T Py 87;L 6;M 6	61 -82 -5 -5	
	J. 0.5	J. 0.5	
	Clinically active		
	X-ray active	Died	
E. D.	3 months		
Aged 32	Sed. R. 0.8	0.8	
	WBC 20,000	19,000	
	B 49;T Py 90;L 4;M 6	64 -87 -7 -5	
	J. 0.5	J. 0.5	
	Clinically active		
	X-ray active	Died	
M. W.	42 months	12 months	
Aged 18	Sed. R.	0.5	0.55
	WBC 20,000	13,000	10,000
	B—Py 82;L 15;M 3	8 -65 -24 -6	3 -57 -34 -7
	Clinically active	Clinically inactive	Clinically inactive
	X-ray active	X-ray ?inactive	No change

x-ray findings. However, they all had moderately active bloods which definitely improved under the sanatorium régime. In extremely doubtful cases, there are considerable data in the literature on the value of the Schilling response following tuberculin injection and this may be a worth while procedure in certain diagnostic predicaments.

REFERENCES

1 Duffy, J.: Activity in pulmonary tuberculosis as determined by comparative study of roentgenograms, blood sedimentation and leucocytic reactions. Tubercle 14: 60 (Nov. and Dec.) 1932.

2 Fahraeus, Robin: Colorless blood corpuscles. Acta med. Scandinav. 60: 12, 1924.

3 Linzenmeier, G.: Kapillar-microskopische Untersuchungen. Zentralbl. f. Gynäk. 46: 1010, 1922.

4 Greisheimer, E. M.; Ryan, M.; and Johnson, O. H.: The relationship between cell count and sedimentation index. Am. J. Physiol. 89: 170, 1929.

5 Cutler, J. W.: Practical application of blood sedimentation test in general medicine: observations based upon approximately 5,000 patients over a period of six years. Am. J. M. Sc. 183: 643 1932.

6 Rourke, M. D., and Ernstene, A. C.: A method of correcting the erythrocyte sedimentation rate for variations in the cell volume percentage of the blood. J. Clin. Invest. 8: 545, 1930-31.

7 Trail, R. R.: Sedimentation rate and ultimate prognosis in tuberculosis. Lancet 1: 522, 1933.

8 Sabin, F. R.: Cellular studies in tuberculosis. Am. Rev. Tuberc. 25: 153, 1932.

9 Schilling, V.: Differential blood counts. Ztschr. f. klin. Med. 99: 232, 1924.

10 Arneth: Arneth's formula. J. A. M. A. (Abst.) 84: 1606 (May) 1925.

11 Medlar, E. M.: An evaluation of the leucocytic reaction in the blood as found in cases of tuberculosis. Am. Rev. Tuberc. 20: 312 (Sept.) 1929.

CHAIRMAN MORGAN: We will now have a summary of these different departments by Dr. William H. Ordway, Physician-in-Charge of the Metropolitan Life Insurance Company Sanatorium, Mt. McGregor, New York State, who will speak on "Discussion and Summary of the Whole Problem with Especial Reference to the Study of the Leucocyte Count in Pulmonary Tuberculosis."

DISCUSSION AND SUMMARY OF THE WHOLE PROBLEM WITH ESPECIAL REFERENCE TO THE STUDY OF THE LEUCOCYTE COUNT IN PULMONARY TUBERCULOSIS*

BY WILLIAM H. ORDWAY, M.D.†

Mr. Chairman, Ladies and Gentlemen:

I APPRECIATE very much your courtesy in asking me to discuss this very important problem of activity in pulmonary tuberculosis.

Activity of a tuberculous process may be defined as that state of the lesion that has for its main characteristic a labile instability, either progressive or retrogressive, which may be reflected on a pathological or clinical basis, or both. On a pathological basis the disease is assumed to progress in a subclinical manner and arouse no suspicions, so far as the patient is concerned, as to the status of his disease. By clinical activity we infer that the pathological activity is no longer latent and that there are certain reactions on the part of the patient to his infection that call attention to the presence of disease.

A careful study of the pathology of pulmonary tuberculosis affords ample reasons for the divergent opinions and interpretations of what constitutes activity. All degrees of progression, retrogression, quiescence, and healing may be present in even a small x-ray lesion, and it may be extremely difficult even for the pathologist with the section under scrutiny to accurately weigh the interplay of reactions. Little wonder, therefore, that the clinician, who must depend upon direct and indirect reactions, many of a non-specific character, should stumble and grope for his bearings. He must rely on second-hand biopsies which bear the imprint of too much handling by diverse forces that may have no participation in delivering the reaction in its original state. It is only by a careful appraisal of all possible scraps of information pointing to a trend that he can discern the course of the disease.

In these studies of activity of the tuberculous process it seems logical to state that our correct interpretations in the end are more or less proportionate to the frequency and accuracy of the tests which to date have given the most reliable information.

To all who have had only a limited sanatorium experience has come the realization that a tuberculous process may spread in an amazing manner without clinical symptoms or signs, at rest or on carefully controlled exercise. If such is the case it can be logically inferred that there must be in our population individuals who, likewise, certainly have no indication that they are harboring a progressive tuberculous process.

In discussion of the first three papers presented by Doctors Wagner, Hunt and Pettingill on symptoms, physical signs and x-ray, I would like to present a study by Dr. H. H. Fellows who has kindly lent to me this material, as yet unpublished, covering a period of six years among our 13,000 employees at the Home Office of the Metropolitan Life Insurance Company in New York City.

About 55 per cent of the entire group is made up of young men and women of not more than twenty-five years of age, and the remaining 45 per cent is made up of men and women up to sixty-five for the females and age seventy for the males.

Every employee is accepted for employment after having passed a satisfactory physical examination, and annual examination of all employees takes place on the anniversary of their appointment.

Beginning in the spring of 1928 a routine fluoroscopic examination was made a part of the usual annual examination of all employees. In instances where the fluoroscope has revealed pulmonary lesions, stereoscopic films have been taken for purposes of record and study, as indicated.

During this period a total of 141 cases of active tuberculosis has been reported. Ninety-three per cent of the total have elected to accept treatment at Mt. McGregor and the remainder has had the diagnosis confirmed by outside agencies. Twenty-one per cent of these patients were between the ages of seventeen and nineteen, 60 per cent between twenty and twenty-four, and 10 per cent were twenty-five and over. Sixty-five per cent were discovered in the minimal stage, 30 per cent in the moderately advanced and 5 per cent in the far advanced. Thirty-three per cent presented no symptoms whatsoever, 9 per cent admitted fatigue after close questioning, 13 per cent had cough, or cough and expectoration, 10 per cent acknowledged slight chest pain, and 13 per cent had had hemoptyses. Sixty-five per cent were symptom-free and had only one symptom suggestive of tuberculosis. Fifty-eight per cent had no râles either at the Home Office or on admission to the Sanatorium at Mt. McGregor. Four per cent had pleurisy with effusion, 45 per cent had lost three or more pounds in weight, 20 per cent had gained three or more pounds in weight, and in 35 per cent the weight had been stationary within a year of the established diagnosis.

*Read at the Annual Meeting of the Massachusetts Medical Society, Section of Tuberculosis, at Worcester, June 6, 1934.

†Ordway, William H.—Physician-in-charge of the Metropolitan Life Insurance Company Sanatorium. For record and address of author see "This Week's Issue," page 285.

Fifty-two per cent were subjected to roentgenographic examination because of a suggestive history only, and 48 per cent were revealed by fluoroscopic or x-ray examination.

Thirty-one per cent of those admitted to the Sanatorium had a positive sputum at some time during their residence.

From this study it is apparent that: (1) a large proportion of cases was discovered in the minimal stage; five times the rate of average admission of minimal cases as reported by Hill and Williams; (2) the majority of cases was detected before patients were clinically active; (3) the majority of cases was diagnosed before physical signs became evident; (4) the fluoroscopic examination at *periodic intervals* and after so-called minor respiratory infection is a valuable procedure; and (5) the confirmatory value of the x-ray to indicate progressive disease.

Another manner of demonstrating that pulmonary tuberculosis can be present without signs or symptoms is in the examination of applicants for employment at our Home Office. Fellows and Reid show that the incidence of pulmonary tuberculosis among one to four thousand such applicants between the years 1928 and 1933 varied from 1.1 to 1.5 per cent. About 50 per cent of these have active pulmonary tuberculosis.

Increased cough and expectoration may indicate a recrudescence, especially where a previously mucoid sputum becomes mucopurulent and where, in some cases, the Gaffky count is appreciably increased. Duffy maintains that a count higher than Gaffky II indicates activity.

Despite the reports in the literature of persistently positive sputa as being consistent with health, it is difficult to divorce one's self from the impression that a positive sputum does not indicate at least a smoldering pathological activity.

Heise, in a study of 300 advanced tuberculosis cases at Trudeau Sanatorium, shows that 48 per cent exhibiting progressive x-ray lesions had positive sputum; conversely, 50 per cent with a negative sputum fell into the stable or unchanging group by x-ray.

Dublin, in a recent study of over 2,000 cases discharged alive from the Sanatorium at Mt. McGregor between 1914 and 1931, shows that in general a high death rate prevails in all cases where there was a positive sputum present during observation.

Comparing these discharged patients with our regular employees of corresponding age and sex it was found that those having a positive sputum had a mortality thirty-three and a half times the expected. Patients with a positive sputum at the time of admission but discharged with a negative sputum had a mortality 310 per cent greater than the expected, whereas those with a negative sputum had a mortality 164 per cent of the expected.

INCIDENCE OF TUBERCULOSIS AMONG APPLICANTS FOR EMPLOYMENT

Year	Applicants	Cases of Tuberculosis Discovered by				Incidence per 1,000	% Discovered only by Fluoroscopy
		Total	History	Physical	Fluoroscopy		
1928	4,405	69	9	7	50	15.6	76%
1929	4,780	57	6	6	45	11.6	79%
1930	3,105	36	3	1	32	11.2	91%
1931	2,175	33	2	4	27	12.4	82%
1932	2,134	32	2	0	30	14.0	96%
1933	1,166	17	3	1	13	14.5	76%

It is apparent that the advance in the eradication of pulmonary tuberculosis has already entered the prophylactic phase and if we are to extend these gains we must look for tuberculosis before it has reached the stage of symptomatology and, in a majority, before physical signs appear.

The constitutional symptoms of fever, rapid pulse, loss of weight, fatigue, malaise, irritability, night-sweats, gastric disturbances, etc., are indications of toxemia and activity.

Localizing symptoms, such as frank pleurisy, wet or dry, indicate an extension of involvement, hence activity.

Hemoptysis should usually be considered an indication of activity, except, perhaps, in the chronic fibroid cases, where it may be due to a bronchiectasis resulting from the tuberculous process but not actually indicating activity *per se*.

Spontaneous pneumothorax in the tuberculous is generally considered as the result of activity, though at times it is impossible to demonstrate such activity by the roentgenogram.

Elastic fibres when found in the sputum always indicate activity.

The illuminating and extensive studies of Brown, Heise and Sampson concerning physical findings show how frequently they may be absent in spite of manifest disease.

In a study of 4,000 school children at Saranac Lake examined roentgenologically over a period of seven years, seventy-nine had parenchymal lesions and only seven had definite signs.

Of 280 minimal cases at Trudeau Sanatorium 27 per cent had râles at the apex, while 99 per

cent had definite parenchymal lesions by x-ray.

In a study of over 1,000 cases Brown found none with definite physical signs and a negative x-ray. Two per cent had physical signs greater than the extent revealed by x-ray. In 21 per cent physical signs and x-ray showed equal involvement of the lung tissue. Thirty-six per cent revealed more extensive disease by x-ray than by physical signs. Forty per cent showed definite evidence of disease by x-ray with normal physical findings.

Brown, studying 503 patients exhibiting only indefinite or no abnormal signs but a parenchymal x-ray lesion with ill-defined borders, showed that sooner or later 84 per cent of these cases presented clear-cut clinical evidence of the disease.

It is well recognized by all that cavity is all too frequently silent from the standpoint of physical signs. Brown and Sampson state that 40 per cent of all patients admitted to Trudeau Sanatorium have cavity and that in 392 consecutive cases with cavity only 15 per cent had physical signs suggesting this condition.

Brown states that an increase in physical signs may accompany a very definite improvement in the clinical condition with a clearance in the roentgenographical shadows. Likewise, physical signs may remain stationary while the x-ray indicates a definite increase. In a certain number the physical signs decreased while patients apparently progressed unfavorably. In many instances both physical signs and x-ray changes in either direction go hand in hand. In some instances physical findings persist years after the lesion is apparently healed.

Serial roentgenograms by far give us the best single examination information obtainable. Shadows with ill-defined nebulous borders seem to indicate activity, while those with clear-cut borders are more liable to indicate an inactive condition.

Such figures as these indicate that the x-ray is superior to clinical judgment as to the determination of activity. In certain instances, however, particularly in the advanced cases with a multiplicity of lesions, it must be admitted that the x-ray has certain limitations because minor progressions or remissions in activity are obscured.

In discussing Dr. Badger's paper it is evident from his studies that tuberculin indicates sensitivity rather than activity and this is quite in accord with our experiences.

When tuberculin is given and an individual is sensitive to it, an increased demand for neutrophiles always occurs at the expense of the lymphocytes. It generally depends on two factors: first, the sensitivity of the individuals; secondly, the dosage of tuberculin. In our experience it has been found that the leukocytic response is more delicate than the general body reaction.

A number of years ago we abandoned the subcutaneous tuberculin test as an unreliable diagnostic procedure, for the reason that about ten cases with suspected or demonstrable parenchymatous x-ray lesions failed to react to a dose of 10 mg. twice repeated and later on developed clinical tuberculosis.

Bredeck reports that with the Schilling count, tuberculin subcutaneously injected gives very definite information as to activity, but to date our investigations, still incomplete, indicate sensitivity rather than degree of activity.

Dr. Kaminsky has outlined Medlar's conception of the leukocyte count in pulmonary tuberculosis, so there is no need for me to repeat Medlar's method of interpretation of this reaction.

It is our opinion that the leukocyte count does afford us a method of obtaining a biopsy, so to speak, of the pathological tuberculous process, and can give valuable information in the treatment and disposal of tuberculous patients.

Considerable difficulty has been encountered by many workers in comprehending the proper manner of interpreting the results of leukocyte studies as propounded by Medlar. Dr. Crawford, of our medical staff, has devised a slide rule by which Medlar's pathological conception can be expressed in the form of an index. A leukocytic index from 0 to 15 indicates a favorable state of the pathology, 15 to 26 slightly unfavorable, 26 and above unfavorable to very unfavorable.

A study of tuberculous patients doing well clinically showed that 57 per cent of the leukocyte counts fell within an index of 0-15 and 43 per cent between 16-26. In those presenting an unfavorable clinical and pathological condition only 8 per cent of the counts were between 0-15, 43 per cent between 16-26 and 49 per cent between 27-100. Those showing a very unfavorable type of pathology showed 2 per cent with an index between 22-26 and the remainder above these levels.

The mortality experience of patients using the index as a guide demonstrates that in the group of 281 studied over a period of six years none with a favorable count have died from the disease, 10 per cent were incapacitated and the remainder were working. In those having unfavorable counts 8 per cent were dead, 38 per cent incapacitated and 54 per cent working. In the very unfavorable group 42 per cent were dead, 27 per cent were unable to work and 31 per cent were working.

The disparity in opinion occurs principally in the unfavorable and very unfavorable cases as determined by the blood when compared with the clinical judgment of the case. It is Medlar's contention that work is not a valid test of a patient's ability to withstand his disease. A patient may carry on at work with a pathologically active process in his lung as reflected in the leukocytic picture and show no clinical evidence of this condition. Certainly the cases having a favorable count show surprisingly few casualties. It should be understood, as well,

that the clinician is constantly thinking of the average case of tuberculosis from the pulmonary standpoint and neglects to recall the lessons learned in the dead house that other lesions, frequently microscopic, may exist outside the pulmonary field in other organs. All this the blood count takes into consideration.

Dr. Muller's paper shows a great amount of study. Whenever any interpretation of a leukocytic reaction is attempted it is essential to bear in mind that it is the proportion of various leukocytic types that comprises the picture. In Medlar's interpretation the polymorphonuclear, the lymphocyte and the monocyte are all concerned in the pathological process at some time during the infection. Some investigators favor the poly-lymph ratio, others the monocyte-lymph ratio. In either instance the significant rôle played by the monocytes on the one hand and the neutrophiles on the other is relegated to the background.

One must remember that the monocyte-lymphocyte ratio may become very abnormal in cases where the monocyte percentage remains normal, whereas the cause for the ratio approaching normal is due to a marked decrease in the lymphocytes together with a proportional increase in the polymorphonuclears. In other instances the same ratio value may be caused by a slight decrease in lymphocytes and in polymorphonuclears with a marked increase in the mononuclears.

I agree, and I think it is generally conceded now, that the monocyte-lymphocyte ratio is not in any sense of diagnostic significance.

Dr. Cass's paper likewise exhibits a considerable amount of valuable research study. It has been shown by Arneth, Schilling and others that, whenever there is an increased demand, for polymorphonuclears over a period of twenty-four hours or longer, one will find an increased number of immature forms of this cell type in the circulating blood. If this demand is temporary, that is, for a few days, the number of immature forms will rapidly disappear from the circulation.

Medlar has shown in his experimental animals, however, that there is generally an increased demand for the young forms at the outset of the infection. He believes that after a period of sustained withdrawal the hematopoietic system may increase in volume to such an extent that the number of immature polymorphonuclears may approach the normal level even while the demand for these cells remains excessive.

While the Schilling count is of distinct value, considering the extra time, the skill required in differentiating the cells, and the possibility of error, it is our belief that, with the possible exception of the acute tuberculous process, it does not give added information that cannot be obtained from Medlar's formula.

It is our impression that the sedimentation test may indicate activity of the lesion but cannot be depended upon to foretell impending disaster. It conforms rather snugly to clinical impressions. Like the leukocyte count we do not believe that in the very early stages of minimal disease it gives as much information concerning activity as can be obtained by serial roentgenograms. In other words, both of these reactions seem to lack definite information when it is most needed and the x-ray has to be relied upon almost exclusively when a small lesion is first discovered. I refer particularly to the small lesion of the apparently acute type occurring in the young adult, similar to the slides I have shown you. With the larger amounts of infiltration both tests may show signs of activity and the intensity of the reaction is more or less proportional to the degree of involvement.

The papers presented here this morning represent a tremendous amount of investigation and study, indicating that the tuberculous patient in late years is receiving more individual study and investigative research.

In conclusion, from a prophylactic standpoint the use of the fluoroscope in large masses of individuals by careful and conscientious investigators can discover small and early lesions which clinically give no evidence of their existence, i.e., when the lesion is pathologically active.

Serial roentgenograms, particularly in the beginning of tuberculous pulmonary infection, may be the only means of demonstrating active tuberculosis.

The young adult with an x-ray pulmonary lesion exhibiting an ill-defined fluffy border merging into a normal pulmonary field should have the benefit of sanatorium observation and treatment. In most instances it is synonymous with an active lesion. Individuals with shadows exhibiting a sharply outlined border interpreted as healed or quiescent lesions, particularly in the adolescent and young adult groups, require periodic x-ray examination at least annually.

While patients are under observation and treatment serial roentgenograms afford the best means of determining activity; next in order of value the leukocytic reactions, red cell sedimentation rate; lastly, physical signs and symptoms. In a disease as complex as tuberculosis no one procedure is infallible, and the best information is obtained by a careful and intelligent interpretation of all methods available that have given evidence of merit.

CHAIRMAN MORGAN: I am sorry that there will be no time allowed for discussion of these papers, because we have already run five minutes over our allotted time. Before we leave, however, I want to thank Dr. Ordway for his very fine exposition on this subject. And I also want to thank the other speakers who have contributed papers here this morning. This meeting will now be adjourned.

(The meeting adjourned at 12.05 p. m.)

NEW HAMPSHIRE MEDICAL SOCIETY

PHENOBARBITAL POISONING*

BY BERNARD P. HAUBRICH, M.D.†

I AM going to discuss the experience I had with a drug which we are all using quite frequently now, phenobarbital (Luminal, Phenylethyl Barbituric Acid).

I was treating a primipara who was six weeks along for morning sickness, with a prescription which contained one-half grain of phenobarbital and about six grains of sodium bromide in a dose, in a vehicle of elixir lactated pepsin, and was giving this dose three times a day. After the patient had been taking this medicine for about two weeks, she came into the office with a fine, diffuse, punctate and rather pale erythema extending over her face, neck, chest, abdomen and back, together with palpable and slightly tender postauricular glands and a fever of about 99.6°. I made a diagnosis of German measles. Nine days later I was called to see this patient for flowing a small amount without any cramps. At this time she was running a temperature of 100°, pulse 100, her blood pressure was 125/70, and she complained of soreness in the glands of her neck. Her rash had not cleared up as yet. The next day (eleventh since onset of the skin eruption), the patient had a fever of 103°, pulse 108, increased postauricular adenopathy, malaise, and was covered with a diffuse, blotchy, irregular-shaped erythema over her chest and abdomen, greatly resembling a measles rash, but with absent Koplik's spots. At that time I omitted the phenobarbital prescription. On the fifteenth day her temperature had dropped to 98.4° and her pulse to 86. Then her nausea and vomiting were bothering again; so I resumed the phenobarbital. Two days later (seventeenth day) the blotchy rash reappeared all over her body, arms, legs, face and neck and she complained of sore throat, dysphagia, headache, sore and swollen eyelids with redness and lacrimation, itching of the skin, fever of 101.5° and pulse of 112, and some nausea and vomiting. At this time all medication was discontinued.

On the nineteenth day her urine examination showed dark coloration, specific gravity of 1.025, alkaline reaction, albumen and sugar absent. Sediment showed few squamous cells and occasional white blood cells. The blood Wassermann was negative. At about that stage of her illness, her scleral conjunctivae appeared yellow and she began to desquamate. Twenty-four days from the onset of the rash she had cramps and began to flow, and within twelve hours she miscarried a ten weeks' fetus without the placenta. The next day the placenta was removed.

At about this period the patient's skin and conjunctivae were of a dark yellowish coloration. She was desquamating in large flakes all over her body. Her urine was dark-colored and showed strongly positive for bile, slight trace of albumen, and was loaded with pus and squamous cells.

On the thirty-fourth day an ischio-rectal abscess, which had been forming for some days, was incised and drained for about a week. By the thirty-eighth day the jaundice was nearly gone, but there remained a blotchy brownish pigmentation of the skin, which faded but did not entirely disappear until almost twelve weeks from the onset. Within two months from the initial appearance of the skin condition the patient felt about as well as ever, aside from the skin pigmentation, and about six months from the onset she became pregnant again. She is now about eight months along and has been doing very well with normal urine and blood pressure and she has been entirely free from untoward symptoms.

To summarize the important features of this case: Fourteen days after a primipara, six weeks along in pregnancy, began taking a prescription containing one-half grain of phenobarbital and six grains of sodium bromide three times a day, she developed a dermatitis, postauricular adenopathy, and fever which appeared like German measles. Eleven days from the onset of these symptoms she had a skin eruption, fever, pulse, adenitis, sore throat, and malaise all of which were consistent with measles except for the absence of Koplik's spots. Four days after the discontinuance of this medication the patient's symptoms had improved, only to be aggravated again by the resumption of these drugs. Two days after resuming the prescription, or seventeen days from the initial skin condition, the patient again manifested the blotchy measles-like rash, sore eyes, conjunctivitis, sore throat, dysphagia, headache, marked restlessness, cough and adenitis. Up to this time when the drug was permanently discontinued, I estimate that the patient had taken a total of about forty grains of phenobarbital and about four hundred and eighty-six grains of sodium bromide. Marked jaundice appeared by the nineteenth day from the onset of the initial symptoms and was followed by profuse desquamation of large thick

*Read before the New Hampshire Medical Society at its Annual Meeting at Manchester, May 15, 1934.

†Haubrich, Bernard P.—On Staff of Claremont General Hospital. For record and address of author see "This Week's Issue," page 285.

scales. Miscarriage of a ten weeks' fetus occurred on the twenty-fourth day. The patient made a complete recovery, but it was eleven or twelve weeks before the skin pigmentation had entirely cleared up.

In reviewing the literature on toxic reactions or idiosyncrasies of the barbituric acid derivatives, it is to be observed that the toxic manifestations are of two types:

1. Those due to reactions from the therapeutic dose.
2. Those due to poisoning from an overdose.

Dougherty, M. S., (*South. M. J.* 25: 1145, 1932), states that the toxic reactions vary from the mildest reaction of lassitude, drowsiness, malaise and giddiness, which many patients complain of a few hours after taking the drug, to profound coma and death. Lancaster, A. H. (*South M. J.*, 25: 1142, 1932) states that it has been estimated that one to three per cent of patients taking phenobarbital developed toxic symptoms showing manifestation in the skin.

1. Toxic Reaction from Therapeutic Dose. It is the class of cases which develop toxic symptoms from the therapeutic dose (idiosyncrasies) that I am chiefly concerned with in this paper. There are two types of skin reactions described in this group of cases: A. Urticarial wheals and itching. This is probably a sensitization reaction. B. Toxic reactions are characterized by a measles or scarlatiniform maculopapular erythema.

The eruption usually begins about the neck, upper part of chest, inner surfaces of thighs and eyelids, and unless the etiological agent is immediately recognized, in a short time will spread over the entire body with marked involvement of the mucous membrane of the mouth and throat. The conjunctiva becomes congested, eyelids swollen, and the entire body becomes covered with a brilliant erythema which itches intensely and in several cases the eruption has developed to the formation of vesicles.

There is usually an elevation of temperature which may go as high as 103° or 104°. It is not unusual to see the temperature as high as 101° or 102°. Concomitant symptoms may be present as gastro-intestinal symptoms of nausea, vomiting and diarrhea. Neurological symptoms of drowsiness, headache and dizziness. Adenitis is frequently observed. The leucocyte count, when varying, is usually raised. It has been observed that phenobarbital dermatitis, as well as scarlet fever, is usually accompanied by an eosinophilia.

If the causative factor in these cases is not discovered and discontinued, the symptoms will become more marked and serious and will stimulate the conditions described below under the reactions from an overdose.

2. Poisoning from an Overdose. In acute poisoning which occurs where a large dose of the barbituric acid derivatives is taken by mistake or with suicidal intent, the symptoms are frequently stupor, mental disturbances, speech disorders, low blood pressure, low pulse, cyanosis, dilated pupils, nystagmus, diplopia, delusions, paraphasia, mild confusion, mild agitation, ataxia, lethargy, aggravation of paroxysmal seizures, coma, loss of sphincter control and at times interference with the respiratory reflex with pulmonary edema and bronchopneumonia.

In the fatal cases there are deep coma, cyanosis, low blood pressure, cold skin, incontinence of urine and feces and finally death from respiratory failure.

The question arises as to the size of the dose which will cause the eruption and when it is to be expected.

Babington reported an eruption in a patient on the second day, who had been receiving one-quarter grain phenobarbital twice a day. The drug was discontinued and the dermatitis cleared up. Upon administering one-quarter grain twice a day again the patient had a recurrence of the eruption on the second day.

Poole reported a woman, aged forty-five, with cystitis, who had received one grain of luminal per day for five months and then six grains a day for six weeks, making a total of three hundred and ninety grains (26 grams) before a dermatitis was noticed.

Zimmerman reported a case who received eighteen and one-half grains (1.2 grams) all in one day and developed a rash on the eighth day. There have been fatalities from taking as low as fifteen grains of phenobarbital, although the usual minimal lethal dose is fifty grains.

The average case clears up in about ten days to two weeks following the discontinuance of the drug, although Babington reported a case in which the eruption appeared one week following the discontinuance of the drug and which was one month in subsiding.

One attack of luminal dermatitis does not necessarily mean that the patient will not be able to again take the drug. Curschmann was able to continue the drug in smaller doses after the subsidence of the rash.

Von Bernuth observed the fading of the rash in two cases without discontinuing the drug and in the third case increased the dose from one and one-half grains to three grains daily with a simultaneous disappearance of the rash.

Poole recommends that a skin test be made by injecting .02 cc. (1/3 minim) of 2 per cent solution (luminal) intradermally. In a case that he tested in such a manner, two minutes following the injection, an urticarial wheal developed. After thirty minutes the area of edema measured 5 x 8 cm. The edema remained unchanged for two hours and then gradually disappeared. The control tests made with physiological salt solutions were negative.

The treatment for poisoning from the derivatives of barbituric acid, until recently, has

been symptomatic, but lately two other important measures have been discovered.

1. Intravenous Glucose. Johnson and his coworkers, while using barbitalized dogs in some work on hyperglycemia, were struck by the rapid recovery of these animals as compared with others not receiving large quantities of dextrose solution. This led them to use diuretic measures in one clinical case of attempted suicide with barbital. The patient had taken sixty grains of barbital and was in a semi-stuporous condition. He was given intravenously 1500 cc. of a 5 per cent glucose solution and in six hours passed 1100 cc. of urine and five hours later showed very few symptoms of the drug. Glucose may be of value in the treatment of luminal dermatitis and is at least worth trying.

2. Coramine. Bleckwenn's investigation, demonstrating that sodium amytal could make accessible the mental states of catatonics and various depressions for analysis and therapeutic suggestion, necessitated the use of a drug to quickly overcome the narcotic effect of sodium amytal.

Hans H. Reece (*Wisconsin M. J.* 32:530, 1933) used a twenty-five per cent aqueous solution of coramine (Pyridine -B- Carbonic Acid Diethylamide) in his experiments for the quick elimination of sodium narcosis and intoxications. Patients in profound sodium amytal narcosis (12-20 grains intravenously) who would ordinarily sleep from ten to fourteen hours, received five cc. of the twenty-five per cent aqueous coramine solution intravenously. Shortly afterwards the respiration became deeper and faster, the blood pressure rose, and the pulse remained about constant. In two to five minutes the patients were awake, yawned and started to talk. Within five to ten minutes they had returned to normal both physically and mentally.

The maximal dose of coramine is not known. Reece has given up to eleven cc. of the twenty-five per cent solution (aqueous) intravenously, but recommends the use of from four to eight cc. to avoid excessive respiratory stimulation, overventilation, and possible convulsions in cases of latent tetany.

Thus the effect of coramine exerted upon the respiratory and cardiac centers in drug narcoses and intoxications is of the utmost importance and should be used as the antidote in accidental, experimental and suicidal intoxications induced by the barbituric acid derivatives.

Conclusions: The various barbituric acid derivatives should have a high place in our drug armamentarium. We all know their worth in epilepsy, pre-operative hypnosis, obstetrics, neurasthenia, morning sickness and for numerous other conditions. These relatively rare idiosyncrasies should not prevent their use under a physician's care, but we should not be unmindful of their untoward effects and should be on the alert to detect any early symptoms of toxicity.

Moreover, these preparations are to some extent habit-forming and should not be available to the laity as they are in most states. There is need of some restriction upon their indiscriminate sale and use and this would probably best be accomplished by having them available only upon a physician's prescription and not allowing refills upon the original prescription.

DISCUSSION

PRESIDENT GRAVES: Discussion will be opened by Dr. Charles F. Keeley of Claremont.

DR. CHARLES F. KEELEY: *Mr. President and Members of the Society*—This paper has impressed me for three reasons. The first is that we realize that in food there are idiosyncrasies. There is no way, other than giving skin tests, to determine beforehand about these patients. Just at the time of the appearance of the rash, it is best, if you see a patient, to consider what he has been taking. Quite frequently, he will come in to your office with a rash, and you will find that he has been purchasing patent medicines containing some of these drugs that are sedatives or those that belong to the salicylates or coal tar products.

The second reason is the type of rash. The rash in drug poisoning resembles almost any rash in dermatology. It will range from a scarlatina straight through to a degeneration of the skin. You will notice this particularly among the bromides and iodides.

The third reason is the increasing use of these drugs, both in surgery and obstetrics. Surgically, they are used as basic anesthesia. For instance, you will find that in all hospitals and among the general practitioners doing obstetrics, these are increasing, and, as time goes on we will have more of the rashes, and, worse than that, we will have the effects of these drugs. Amytal is a drug that I have been using considerably but I have come to fear it, particularly after surgery. In administering it, before our cases have had an anesthetic, they seem to have no effect, other than sedative, but anywhere from forty-eight hours to seven days after, I have noticed that the patients have lacked judgment and have even had to be restrained. They had taken the drug previous to ether without any effect, but after the administration of the anesthetic, they have had a delirium lasting four to seven hours after the drug. I thank you.

PRESIDENT GRAVES: The paper is now open for general discussion.

DR. COBURN of Manchester: There are one or two points which Dr. Haubrich brought out in his paper about which I would like to speak. First, that we have no law in this state preventing anybody from buying barbital preparations. I think we should all mark our barbital preparation prescriptions WNR and give only as much as we think the patient will need for a short period of time, to accomplish or test out their reaction and also the therapeutic effect. My custom has been to mark all barbital preparations WNR, which prevents the patients from handing it to their neighbors who do not sleep.

There is one other point I would like to make. Phenobarbital is not very soluble. I think that in making up liquid preparations where phenobarbital is used, the sodium salt, phenobarbital sodium, should be used. Otherwise, if you have a fairly large dose, it is not soluble, and if the patient does not shake the bottle each time he takes it, there will be an increase in the dosage. I think if the sodium salt is used, it will obviate that point.

PRESIDENT GRAVES: Is there any other discussion? If not, I will ask Dr. Haubrich to close the discussion.

DR. HAUBRICH: I have nothing more to add except that I might say that in going over the literature I found no other cases reported with barbital poisoning during pregnancy. I also failed to find jaundice reported in the symptoms of most cases. Probably the pregnancy aggravated this condition.

BONE TUMORS*

Report of Two Cases of Benign Giant Cell Tumors

BY HERBERT L. TAYLOR, M.D.†

I HAVE not gone into the etiology, but it is my firm opinion that trauma of some sort may be surgical, infectious or otherwise producing irritation and disturbance of the normal functions of the body cell is the main background in all bone tumors. The subject is so vast that it is impossible to cover the subject in such a paper as this.

After this paper I have a few lantern slides to show the progress of the tumor up to the time of operation and the gradual filling in of the bone cavity with new bone.

The skeleton may be the seat of multiple lesions and yet only one lesion may attract the attention of the host by pain or swelling, therefore it is a good plan to examine all bones. When the x-ray shows multiple, distinctly central lesions we can practically exclude primary sarcoma and the diagnosis rests between metastatic carcinoma, multiple myeloma, multiple bone cysts and chondroma, and an exception might be Paget's disease.

An x-ray of the chest should be made, as metastases to the lungs are frequent.

If a patient has tuberculosis of the chest, the bone lesion is apt to be the same. If the tumor is hard it is not sarcoma, because sarcoma is apt to be soft on feeling through the soft parts.

X-ray may show tumor when palpation cannot show involvement of periosteum outside the cortical layer of the bone. Other routine examinations are the Wassermann test, complete blood examination, an examination of the urine for Bence-Jones bodies and a search for foci of infection in the tonsil, nasopharynx, teeth and in the genito-urinary tract.

The urine should be repeatedly examined for Bence-Jones bodies. Their presence indicates multiple myeloma or metastatic cancer. When the x-ray shows an evident periosteal lesion and the Wassermann is negative, I advise at least one dose of intravenous salvarsan.

If the x-ray shows a distinct central lesion with definite bone shell, with or without fracture, and no extra-osseous soft-part lesion, and if palpation reveals nothing and the patient is under fifteen years of age we can be quite certain that it is not sarcoma or any other malignant tumor. The probability is that it is a bone cyst and the next possibility is a giant-cell tumor, rarely a chondroma and in a few instances tuberculosis. One can watch the control by frequent x-ray examinations.

Operation promises rapid permanent ossification if it is a bone cyst and it is the best treatment for either giant-cell tumor or chondroma. If the patient is over fifteen years of age and x-ray shows evident central lesion with a definite bone shell, nothing is to be gained by delay. Sarcoma cannot be excluded. A single central lesion may be the onset of multiple myeloma, before Bence-Jones bodies appear in the urine, and in which other foci in the marrow do not show on the film. Then too, it may be evidence of metastasis from concealed primary malignant tumor especially in the kidney and prostate.

The order of frequency after fifteen years of age is benign giant-cell tumor, bone cyst, sarcoma, chondroma, and myxoma. The removal of the malignant growth presents the possibility of implantation in other structures and is therefore attended by definite danger. For this reason under the Esmarch bandage expose the bone shell and open it with the electric cautery, and if it is not a cyst remove the tissue within the bone shell, using the hot iron as a curette. Swab the cavity with carbolic acid and alcohol if it is not a cyst. The cavity is packed with fifty per cent zinc chloride gauze. Also implant or otherwise apply radium in the cavity. Resection with the cautery knife is the operation of choice in malignant cases.

The probability of a cure of a central sarcoma after amputation is less than ten per cent. The cauterization must be by actual cautery and also chemical cauterization.

Amputation rarely cures central sarcoma because of metastasis to the lungs. It is also difficult to differentiate sarcoma, cyst and giant-cell tumor. Periosteal sarcoma has less than four per cent of cures after amputation.

Myeloma is rapidly affected by radium and high voltage Roentgen rays, causing rapid dis-

*Read before the New Hampshire Medical Society at its Annual Meeting at Manchester, May 15, 1934.

†Taylor, Herbert L.—Member of the Staff, Portsmouth Hospital, Portsmouth, New Hampshire. For record and address of author see "This Week's Issue," page 285.

appearance of the tumor. Multiple growths always require the above treatment. The frequent locations are the spine and sternum. Solitary myeloma in the long bones require amputation.

Many benign periosteal lesions resemble sarcoma. The benign periosteal lesions are ossifying periostitis, traumatic, infectious, syphilitic, tuberculosis, exostoses and some rare examples of osteomyelitis.

Central sarcoma shows a little better prognosis than periosteal sarcoma. The former grows less rapidly than the latter. The most characteristic feature of the x-ray of a bone cyst, a central giant-cell tumor, or a central sarcoma, is the absence of new bone formation in the periosteum covering the expanded and thin shell present in this case. Myxoma, central or periosteal, should be classed with, and treated as a sarcoma, because it always recurs.

When the x-ray shows a central or marrow lesion, the probabilities are three and a half to one that it is a benign tumor.

In all adults the possibility that the bone lesion is metastatic should always be borne in mind.

Chondroma (a benign tumor) remains stationary for years until an incomplete surgical operation, or some other kind of intervention, such as trauma leading to an increase of vascularity of the tumor takes place, when the tumor rapidly acquires the characteristics of an osteogenic sarcoma. Grossly these tumors do not seem to involve the cortex at all. However, the local recurrence and later metastasis and death prove the malignant nature of the tumor.

These tumors are large and have apparent capsules. Degenerative changes and cyst formation are frequent findings in them. That the pathologist and surgeon are not sufficiently informed about this type of tumor is indicated by the instances of erroneous prognoses given. These growths at times extend into the bone marrow and must be chiseled out, or a resection done in order to effect a cure if possible.

Central chondroma is treated by curetting, cauterization and radium. Periosteal chondroma is composed chiefly of cartilage.

X-ray showing a fuzzy shadow with slight destruction of the cortical bone or a typical radiating formation of periosteal bone, allows a positive diagnosis of some group of sarcomas.

Many amputations and extensive resections have been done for benign lesions, especially bone cyst and giant-cell tumor. Many surgeons have the wrong impression as to the probabilities of cure of them, because such cases have remained well after a diagnosis of sarcoma.

Experience has shown, however, that the results after disarticulation of the hip in osteogenic sarcoma do not differ from amputation distal to the hip joint so far as secondary growths and recurrences are concerned. Inefficient radiation may stimulate the tumor growth; overradiation is dangerous for normal structures of the organism. The skin becomes bronzed and leathery, and ulceration of the skin may ensue. The bones become sclerotic, ivory-like, and spontaneous fractures of such bones evince a definite delay in union; obliteration of the marrow cavity and capillaries of the periosteum cause a scarcity of callus formation in fractures. The influence of radiation on metastases makes the growth melt away in many instances.

At the Bloodgood Clinic for sarcoma of bone, patients are given preoperative irradiation in all bone lesions which are suspicious of malignant disease, and this preoperative irradiation is carried over a period extending up to three months. When they operate, if the lesion is in the upper extremity, it is frequently quite possible to do a resection and later a transplantation of bone.

In the lower extremity, when it is necessary to take out a piece of bone, amputation gives a better functional result than resection with bone transplantation.

Surgeons have always been of the opinion that, when amputating, it is not necessary to go so high as the hip joint, but only high enough to give the tumor sufficient margin of soft parts and bone. An extensive mutilating operation gives no better results than that referred to above. In metastatic carcinoma of bone they usually depend entirely upon irradiation.

Giant-cell tumor is a low-grade neoplastic process, usually single, sometimes multiple, affecting mainly the epiphysis of long bone, but appearing in almost any bone of the body, producing a multicystic excavation with widening of the shaft, and pursuing a prolonged and generally a progressive course, failing to yield metastases.

Spontaneous cure is sometimes observed, but the natural termination is death from hemorrhage and infection, after the growth has reached large dimensions and caused much destruction of bone.

The knowledge of this disease dates from the time of Ambroise Paré who recognized benign tumors of the maxillae which were curable by repeated excision.

Nélaton in 1863 gave a very full description of the gross, microscopic, and clinical features of the disease, including most of our present knowledge. The proliferation of giant-cells must be the essential feature of the process and must predominate and not be scarce in the tissue, since such cells are occasionally seen in other tumors. He recognized the varieties. (1) Typical reddish brown tumors. (2) Fibrous forms. (3) Yellow tumors infiltrated with fatty material. (4) Also very vascular growths yielding a bruit.

The tumor may even be benign with a few fibroblasts and even spindle cells.

In America, Gross in 1879, described in detail the features of giant-cell tumor, analyzing seventy cases and emphasizing their benign character.

Nevertheless most of the tumors were treated as malignant processes until Bloodgood in 1910 again emphasized their benign character and recommended the use of the term "giant-cell tumor" and in 1919, reported forty-seven cases treated by curettage without recurrence.

The tumor causes excavation of the cancellous tissue and a protrusion and thinning of the shaft, while the periosteum long remains intact, and lays down new bone as the tumor enlarges.

The line of demarcation from the unaffected bone is very sharp. The tumors occur most frequently in the lower end of the femur, upper end of the tibia and lower end of the radius, while they may appear in vertebrae, pelvis, or humerus. Practically no bone of the body is exempt.

Diagnosis by x-ray:

The response to radiation of giant-cell tumors is of much diagnostic value, since these tumors respond by slow absorption, while osteogenic sarcoma is resistant.

Herendeen claims that most all cases may be controlled by x-ray therapy and the limb restored to a good functional state.

CASE 1.

MRS. G. B., white, aged 59, clerk. Onset May, 1931; eight months ago. Swelling of right sternoclavicular joint in October, 1931; three months ago. She had pain at the head of the right radius and elbow after massage by an osteopath. She also complained of pain in left knee.

It is noted that she had a cyst of the pancreas removed in 1901; the tonsils were removed in 1928; and the teeth were x-rayed in 1927. At the age of ten she had right otitis media. The menopause occurred at age of 56, three years ago.

Examination: Swelling of the right sternoclavicular joint; swelling and tenderness of the upper end of right radius; swelling and fluid of the left knee joint. The urine was essentially negative including examination for Bence-Jones bodies.

R. B. C. 4,150,000. W. B. C. 4,600. Hgb. 80 per cent. Differential normal. Wassermann weakly positive—Kahn, negative. Later examination after provocative salvarsan, negative Wassermann and Kahn.

In this case the diagnosis is bone disease, and the first x-ray taken suggests syphilitic non-suppurating osteomyelitis of the right radius near the elbow.

November 16, 1931, x-ray shows a well-defined area of osteoporosis involving the head and shaft of the radius for a distance of about 3 cm. The lesion is diffuse in the sense that it is both periosteal and central. There is no visible soft tumor superimposed, but there is very slight new periosteal bone formation.

From the x-ray above we would think of primary osteogenic sarcoma, metastatic carcinoma and syphilitic non-suppurating osteomyelitis.

The film of the right forearm taken January 5, 1932 shows the area of osteoporosis in the radius increasing with more periosteal bone formation.

The first treatment in this case should be antiluetic, then if no improvement is noticed deep x-ray treatments over the lesion of the elbow for three or four weeks. Another Wassermann test should be made after a provocative salvarsan.

There is no reason for operation yet. X-ray films were taken February 17, 1932. The lesion at the upper end of the radius was considerably larger, and is now larger than a silver dollar, consisting chiefly of an area of localized osteoporosis; the shaft of the bone below appears normal, and no involvement of the joint is seen.

Three or four deep x-ray treatments were given at weekly intervals but the tumor continued to enlarge, and the x-ray had little if any effect on the growth.

If the tumor at frozen section be inflammatory, luetic or otherwise, curette, and follow by chemical and thermal cauterization.

If it is primary or a metastatic malignant tumor, employ general anesthesia, and resect the radius with as good a margin as possible, using the electric cautery.

This can be done without injury to the vessels and nerves. Resect the shaft well below the lesion. Operation was performed April 14, 1932.

Postoperative diagnosis: Giant-cell tumor at head of right radius.

Preoperative diagnosis: Sarcoma head of right radius. Gas-Ether Anesthesia.

Operation: Resection of upper one-half or three-fifths of right radius.

Gross pathological findings: Epiphysis of radius intact, oval-shaped tumor about two by three inches, just below epiphysis and destroying shaft of radius for about three or four inches. Tumor surrounded by thin capsule and moderately adherent to surrounding tissues, many vessels of various size entering the tumor the mass of which was soft, with no glandular enlargement.

Operation: Double twenty-four hour preparation of upper extremity, tourniquet applied near axilla. Cautery knife incision from above radio-humeral articulation, for eight inches downward, along the shaft of the radius. The muscular attachments, radio-humeral ligaments and radio-ulna ligaments were cut away from the shaft of the radius. The shaft of the bone was resected by means of a Gigli saw. The tumor mass was exposed and by retractors the tumor was dissected from surrounding structures by means of a cautery knife. After removal, the wall of the cavity was cauterized with the actual cautery. The wound was sewed up with continuous silk, sterile dressing and right angle posterior splint and sling, to keep the arm quiet.

Drainage: Iodoform gauze wick.

Discharged, May 2, wound nearly healed. Results good.

Frozen sections show a very cellular tumor with a number of areas in which the giant-cells predominate. The cellular tissue in between the giant-cells is of a granulation tissue type, and not the sarcoma type. Even in the areas in which giant-cells do not predominate the cellular tissue is of the benign type; that is, the cells are smaller and differ in size and shape. There are both round and spindle cells from the type we see in granulation tissue.

Recurrence necessitated an operation July 31, 1933.

Under local anesthesia, and by means of cautery knife a return of the giant-cell tumor was removed by means of skin incision over the growth, in the region of the upper end of the radius. The tumor was dissected from surrounding tissues by means

of a cautery knife. The cavity was treated by actual cautery and closed by silk. No drainage.

The growth removed by the second operation, sent to Dr. R. E. Miller of Dartmouth College, revealed unorganized accumulation of giant-cells, some of which are in mitoses. About the border of the tumor are strands of fibrous tissue containing macrophages filled with brown pigment. This seems to be the type of tumor which responds slowly to x-ray treatment.

I cannot account for its return as the tumor was beautifully resected with a portion of the radius. No bone shell remained, but there was a capsule. Pathological report of the growth removed at second operation shows a benign giant-cell tumor.

At the present time there is no evidence of return of the growth. X-ray just before operation showed a tumor about one inch in diameter near the external condyle of the right humerus and the head of the radius.

CASE 2.

F. H., aged 18, male, while walking on the floor stepped on waxed paper, twisting the left knee and striking it upon the corner of a wooden box.

The accident occurred December 2, 1932, followed by inability to walk on the leg from the date of the accident.

X-ray showed oblique fracture into the joint and a bone cyst of the upper and outer part of the left tibia. A posterior splint was applied with rest and icebag to the knee joint.

Later deep x-ray therapy at ten-day intervals was employed. Three treatments in all were given, but the tumor steadily increased in size.

The patient had never had any injury to the knee or any pain about the left knee joint before the date of the accident.

In this case the diagnosis is a question between benign giant-cell tumor and benign bone cyst. (Osteitis fibrosa.)

From an x-ray standpoint this is a benign bone cyst or a benign giant-cell tumor. The involvement of the epiphysis is more in favor of a giant-cell tumor.

Eighteen years is a little old for a bone cyst, but still bone cysts do occur at this age. It may have been latent. The history shows that the patient had no previous symptoms.

The involvement of the epiphysis is unusual for a bone cyst; however, Dr. L. Clarence Cohn of the Bloodgood Clinic, Baltimore, Md., in the past year has operated on a bone cyst in just this location in a woman aged 36.

The opposite knee, pelvis, lungs, and skull were negative from an x-ray standpoint. The nose and throat examination:

R. B. C. 4,580,000, W. B. C. 6,200, Hgb. 90 per cent. Eosinophiles present, basophiles few. Wassermann negative.

The urine after repeated examinations was negative for Bence-Jones bodies. The treatment for the fracture was immobilization with posterior tin splint, also this type of patient should be given a course of deep x-ray treatment once in ten days, because if this is a giant-cell tumor x-ray may produce ossification and healing. In these cases it had no effect whatsoever.

If it is a benign bone cyst, the chances are that x-ray treatment will not have much effect.

Regardless of what the tumor is, there should be preliminary irradiation and if there is no ossification there should be an operation. If it is a bone cyst one can let out the fluid, curette the connective tissue lining, and crush the bone shell, dropping the pieces into the cavity. If it is a giant-cell tumor, Bloodgood suggests curetting with cautery; followed by chemical cauterization with carbolic acid and alcohol followed by fifty per cent zinc chloride, and to hasten ossification, chips of bone can be chipped from the tibia below and dropped into the wound.

Operative Record:

Postoperative Diagnosis: Giant-cell tumor of tibia (left upper end).

Preoperative: Tumor of tibia (left upper end).

Gross Pathological Finding: Swelling and tenderness of upper and outer end of left tibia, parallel with patella tendon.

The bone was soft in this locality and the whole upper two and a half to three inches was filled with a soft tumor mass resembling Hamburg steak. The cortex of the bone surrounding the tumor mass was about one-sixteenth to one-eighth inch in thickness.

Operation: Twenty-four hour preparation. Tourniquet applied above the knee. Three-inch incision made over the upper end of tibia parallel with the patella tendon, starting at about the level of the upper end of fibula; the cortex of the bone was opened by means of chisel and enlarged by rongeur forceps, making an opening about one inch wide and two inches long in the cortex. The tumor mass was removed by means of the curette and sponge forceps, particular care being taken to remove all of the mass from the cortex and loose pieces from the anterior of the cavity. The cavity was washed out with hot salt solution and wiped dry with gauze. It was cauterized with strong carbolic acid and alcohol.

A four-inch incision was made over the shaft of the tibia below; the periosteum was incised and separated from the surface of the bone and by means of a chisel and hammer about two teaspoonfuls of chips were removed from the cortex and inserted into the cavity at the head of the tibia. The bone cavity slowly filled with blood. The periosteum and ligaments were closed with No. 2 C. catgut, and the skin closed with silk. No drainage. The wound over the shaft was closed, the periosteum with plain catgut No. 1, the skin with interrupted silk. No drainage. Sterile dressing applied. Posterior wooden splint was applied to the entire leg from the thigh.

Pathological Report by Dr. E. Miller.

Gross report: Several irregular firm rather friable pieces of reddish brown tissue.

Microscopical examination: Many giant cells of the benign type imbedded in a dense fibrous tissue matrix in which is also some pigment, and there are several accumulations of clear vacuolated macrophages. A few eosinophiles are seen. There is no evidence of malignancy.

Pathological Diagnosis: Benign giant-cell tumor of bone.

The follow-up x-rays taken at various times show the bone chips in the cavity of the tibia; also the gradual filling in with new bone.

At the present time the cavity of the upper end of the tibia seems to be completely filled with new bone. The patient is working, has no pain and has made a perfect recovery.

CONCLUSIONS

1. Bone cysts, giant-cell tumor, chondroma and the like require thorough curettage, cauterization and in the case of the cysts crushing in of the bone shell. To hasten ossification in giant-cell tumor and chondroma, bone chips may be inserted into the cavity to hasten formation of new bone.

2. Sarcomatous tumors of bone on account of the poor results of extensive mutilating opera-

tions should be treated in a conservative manner. Extensive x-ray treatment for three months followed by resection and bone grafting of the upper extremity and amputation well above the seat of tumor formation of the lower extremity.

3. Cancer should be treated by the x-ray and no operation performed.

4. The malignant cysts, myxoma, and myelomas require resection or curettage with cauterization and bone chips, either from bone shell or the tibia to hasten ossification.

5. Taking everything into consideration, careful study of the case and conservatism should be the rule.

I wish to thank Dr. Joseph C. Bloodgood and especially Dr. Clarence C. Cohn of the Bloodgood Clinic for the helpful aid in these cases; also Dr. Ezra Jones of Manchester, N. H., for his expert advice, Drs. S. T. Ladd, George Treddick and W. P. Clare for assistance at the operations, and Dr. H. O. Chesley for the x-ray work. Moreover if this paper is helpful to you, I shall feel well repaid for the time required in its preparation.

REFERENCES

1 Bloodgood, Joseph C.: Diagnosis and Treatment of Benign and Malignant Tumors. Baltimore, Maryland.
2 Kolodny, Anatole: Bone Sarcoma. The Primary Malignant Tumors of Bone and The Giant Cell Tumor. Chicago, 1927.
3 Ewing, J.: Neoplastic Tumors. Philadelphia, 1919.
4 Coplin, W. M.: Manual of Pathology Including Bacteriology, the Technic of Postmortems, and Methods of Pathologic Research. Philadelphia, 1910.
5 Gray's Textbook of Anatomy Descriptive and Surgical. Thirteenth Edition. Philadelphia.

DISCUSSION

PRESIDENT GRAVES: I will ask Dr. Jones of Manchester to discuss this paper.

DR. EZRA A. JONES: I understand that Dr. Taylor has called our attention to a most interesting subject. I was fortunate enough to see the tibia, with Dr. Taylor, shortly after the fracture. It was not an easy one to diagnose, but from the fact that it did invade the epiphysis, it probably was a giant-cell tumor. I think that all of these tumors should be studied thoroughly and promptly. The American College of Surgeons has a Bone Sarcoma Registry, which has been a great factor in helping the classification and study of these tumors. As you know, they request that you send cases to them, sending specimens and x-rays, and you can receive advice.

A few years ago, Dr. Codman of Boston was on this Sarcoma Committee, and I was in communication with him about a case. In a letter wherein he gave me advice as to the diagnosis and treatment, he said, "Whatever you do or don't do, don't fail to report it." This particular case was a giant-cell tumor, in the same region as that of Dr. Taylor's patients, but it had progressed so far that amputation was necessary. This probably would not have had to be done, had it been diagnosed a year previously.

My experience with them is that they do pretty well with the heavy voltage x-ray machine.

One case of giant-ceil tumor which I think is interesting was in a patient sixty-four years old, in the inferior ramus of the pubis. He had four x-ray treatments, and had remained well for five years.

With cysts, I had rather an interesting experience which makes me careful of them. A girl eleven years old came in with a knock-knee, due to a cyst in the lower end of the femur. An osteotomy was performed to correct the deformity, and also to break down the cyst walls. This cyst was very slow, but did eventually heal. A year later, she came in with the same condition in the other knee. X-rays at that time showed a marked decalcification of all of her bones, and high blood calcium. This case proved to be a hyperparathyroidism, and later she had an adenoma of her parathyroid, which was removed.

CHAIRMAN LORD: The discussion on this paper will be continued by Dr. Samuel T. Ladd of Portsmouth.

DR. SAMUEL T. LADD: Bone tumors, with their frequency of occurrence, their destructive processes and rapid extension, with loss of limb and life, the difficulty of prognosis, render them one of our great problems of surgery. These tumors are the most rapidly growing neoplasms in the body, and while most of them have certain characteristics which can be classified, yet with the inflammatory processes, the physiological regeneration of bone and infection, all going on at the same time, make your classifications difficult at times.

Astley Cooper first recognized the distinction between periosteal and medullary tumors of the bone and the older clinicians imperfectly; between primary sarcoma, secondary carcinoma and chronic inflammation, and it was not until 1845 that Lebert first microscopically distinguished sarcoma from carcinoma.

Then in 1860 Nélaton brought out the recognition of medullary giant-cell tumors as a special group which were benign. In 1879, Gross reviewed the history and morphology of bone sarcomas, emphasizing, against Billroth's opinion, the benign prognostic importance of giant-cell structure which was up-to-date. Gross's description and classification stands as a classic on this subject. Then again, in 1920, Codman established a registry of bone sarcoma which created a wide interest in America. This has brought out information and important facts, tentative classifications and special studies have been made by leading pathologists and surgeons.

Christensen in a report and tabulation of one thousand cases shows some very interesting facts in regard to sex, age, and distribution.

He shows that osteogenic sarcoma reaches its acme at the fifteenth year, and thereafter declines rapidly. However, a few cases are noted as late as the eighth decade.

Giant-cell tumors occur more frequently in the third decade, endothelial myeloma is noticed more often in early life; more than fifty per cent occur before the twentieth year and many in the first decade. Osteogenic sarcoma is much more frequent in males than females; giant-cell tumors are about equally divided between the sexes, while endothelial myeloma is more frequent in males than females.

The youngest osteogenic sarcoma of Dr. Codman's registry was in a girl of ten months, in the left tibia. Dr. Ewing's case of an endothelial myeloma of pubes and skull was a girl baby eight months old. In children, ninety per cent of bone tumors fall in about these percentages, osteogenic sarcoma forty-eight per cent, giant-cell sarcoma, forty-six per cent, and endothelial myeloma twenty per cent.

Dr. Christensen in his 1000 cases shows in his tabulation that any bone of the body may be the seat of a tumor. He also shows, under the osteogenic type, the number of the benign and malignant tumors and location, and well shows the predilection of these tumors. The femur, tibia and humerus

far exceed all others. That the knee is much more common than any other joint of all types of tumors, is because it is so often subject to trauma. The real cause has never been proved, and recently the Mayo Clinic is claiming that hyperparathyroidism is one of the causes, and removal of the parathyroid bodies often cures these tumors.

Highly important from the diagnostic and etiologic standpoints is the predilection of osteogenic sarcoma for the ends of the diaphysis; of giant-cell tumors for the epiphysis; of the endothelial tumors for the shaft of long bones and the multi-myelomas for the flat bones. It is significant that osteogenic and giant-cell sarcomas occur mainly in the ends of long bones, where the growth period is longest, where natural momentum of growth is greatest, and exposure to trauma is the most common. The deltoid insertion in the humerus is a common point of tumor formation, due to muscular pull, which is the probable causative factor.

Multiplicity probably favors myelomata, whereas in the osteogenic variety rarely have these been recorded, and very few of the endothelial type. The necessity of recognizing the great variation, the natural history, signs of radiography and results of treatment of these different bone tumors, and adoption of classifications based upon these facts are emphasized by the experience of Codman in collecting 700 cases from the American clinics. By this study, it was brought out that the knowledge of the disease is very meager, the treatment generally haphazard, and only twelve cases of five-year cures were tabulated and that this subject challenges the mettle of the profession; if these cases are to be treated scientifically and successfully, especially trained men should deal with this subject. It is evident that the classification is paramount; that the main types should be recognized, to enable one to make a correct prognosis. The three great types are osteogenic, giant-cell tumors and myelomas, and it is for us to discuss the giant-cell tumors which are to-day recognized as being benign.

As has well been pointed out in Dr. Taylor's paper, these giant-cell tumors are of low-grade neoplastic process, usually single, affecting mainly the long bones at the epiphyses, but may appear in any bone producing multicystic excavation, widening of the shaft and never yielding metastasis, sometimes cured spontaneously, but generally if left without treatment terminate in death through hemorrhage and infection.

In 1827, Berchard described a bone medullary tumor which was vascular and non-cancerous. Warren, in 1837, described a malignant and benign tumor of the maxillae, as well as central tumors of the tibia and femur, and it was Lebert who first described the giant-cell tumors of the medullary bones, and again in 1850 Robin brought out the fact that giant-cells predominated in these benign tumors. In England, Paget applied the term "myeloid".

In 1879, Gross gave a detailed description of giant-cell tumors and declared them benign, but was severely criticized by the profession and it was considered poor surgery if all sarcomata were treated otherwise than malignant, and not until 1910, when Bloodgood brought out his report of seventy-nine cases of benign cell sarcoma was the problem made clearer.

The typical giant-cell sarcoma is found in the epiphysis of long bones. Generally first found, because of examination, by radiography for some other injuries, or clinical symptoms, such as pain in the bone, tumor formation and deformity; also pain on motion.

The x-ray is the most certain means of diagnosis. Generally these tumors start from the medullary cavity of the bone, and are destructive. No attempt at new bone formation is found except under the periosteum over the tumor. Under the microscope cystic degeneration of the medullary canal is seen with numerous capillaries mingled with endothelial cells, and giant-cells predominate, giving to the eye an appearance of a gelatinous substance varying in color from a deep red, grey and yellow. Where a few giant-cells are present, spindle cells predominate, the tumor indicates considerable growth capacity and tendency to a recurrence, then your diagnosis should be well guarded, for here you are dealing generally with a mixed tumor which is not benign.

Treatment: That which Dr. Taylor followed in these two cases, which he has so ably reported, is not unlike that which Dr. Bloodgood uses, and I am greatly indebted to Dr. Taylor in allowing me to assist him on both of these cases. The management and the end-results are most gratifying.

I was fortunate enough to be at Dr. Crile's clinic last fall, saw a case of myelomatous sarcoma operated on and heard Dr. Sheehan, who operated, give an exposé of this subject. He brought out the gravity of amputating the arm at the shoulder joint for this type of tumor, and stated that such an operation stimulated the sarcomatous growth in the distal end of the clavicle and the scapula. He showed us, under the microscope, slides that had been taken from each and every case from these two bones and demonstrated the metastases in the clavicle and scapula.

Conclusion: Differential diagnoses must be made. The prognosis should always be guarded unless giant-cells predominate. The treatment is very satisfactory in giant-cell tumor; in other forms of sarcoma only prolonging life.

Chairman Lord: The paper is now open for general discussion.

Dr. Foster of Manchester: I have been interested in this sort of thing for some time, and I feel that giant-cell tumor is an adult disease, the majority of cases occurring perhaps in the third decade, causing a great deal of anxiety at a time when, perhaps, it might be considered on the border-line between benign and malignant growths. There is an analogy between this type of growth of bone, giant-cell tumor, and the solitary bone cyst. We must not forget that a rather large per cent of these giant-cell tumors are the source of spontaneous pathological fracture.

I want to say a word relative to malignancy. Probably on the whole, these cases are benign; nevertheless, a certain number of them treated surgically recur. We must not forget that. There is a possibility of a cyst in giant-cell tumor.

Chairman Lord: Are there others to discuss this paper?

Dr. George C. Wilkins of Manchester: X-ray therapy has a unique position in the treatment of giant-cell tumors of the bone, and it must not be overlooked. In the first place, the treatment of the deep therapy machine will cure the tumor. In the second place, it is a great diagnostic aid, between the giant-cell tumor and the osteogenic sarcoma. The osteosarcoma is a malignant disease and is not helped by x-ray. Giant-cell tumor is a benign growth, which can be cured by deep therapy. That is the importance of the x-ray relationship to this growth.

Chairman Lord: If there are no others to discuss this paper, I will ask Dr. Taylor to conclude.

DR. TAYLOR: The main point in tumors of the bone is to make a diagnosis, as early as possible, and, of course, to render treatment immediately. Most of us, perhaps, don't make the diagnosis early enough and try several different forms of treatment before we get down to the correct one. Sarcomas of the bone are very bad and very fatal. Personally, I have not had a great deal of experience with them, but from what I can read, the deaths from bone sarcoma are not because of the locations. They are from metastases, and it makes little difference whether you do a resection or an amputation at the joint, or, if you have a sarcoma of the humerus, whether you do the amputation at the joint, resection, or remove the scapula with it. You are going to have a return in practically all cases, regardless of what you do. With the giant-cell tumor, from what I have been able to read, I can't quite agree with Dr. Wilkins, that deep x-ray therapy cures all cases of giant-cell tumor. It does cure a good many of them, destroys the cells, forms fibrous tissue, and in a good many cases, later on, bone formation takes place. Myeloma occurs mostly in the skull and spine, where any operative procedure is impossible and the only agency to employ is x-ray or radium.

Chondroma, of course, is very serious, especially if it is not operated upon at once, or if the operation in the beginning is incomplete.

OBSTETRICS IN GENERAL PRACTICE*

A Review of 1,000 Cases

BY B. F. MACCHIA, M.D.†

OBSTETRICAL conservatism, from the Latin derivation and definition of each of these two words, means the art and practice of caring for a woman during pregnancy, parturition and puerperium with the object of preserving and protecting her from injury and destruction.

Labor, as applied to obstetrics, has a reference to the work a pregnant woman has to undertake to bring about the expulsion of a fetus from the uterus. Labor is essentially a normal and conservative process of nature.

The management of labor is that part which the obstetrician undertakes, keeping in mind and applying the underlying principle and intent of the term "Obstetrical Conservatism", and means that he is to stand by and watch this normal process of nature, and undertake to assist this process only when the resources of nature prove inadequate, for some reason or other, to bring about a happy and successful ending. The management of labor means waiting and observing, and not interfering with the natural process.

A recent investigation, by a committee on maternal mortality of the New York Academy of Medicine, revealed that more than one-half the deaths of mothers in childbirth in New York City were preventable. The report further states that "61.1 per cent of the preventable deaths are the fault of the medical attendant", and that these deaths "have been brought about by some incapacity of the attendant such as lack of judgment, lack of skill, or carelessness". It also states that there was a prominent increase in the proportion of operative deliveries, that operative deliveries amounted to 24.2 per cent of the cases against an authoritative estimate that not more than 5 per cent of all deliveries require operative interference; and that "the increased hazard from these operations represented a serious defect in the management of labor".

If a policy of watchful waiting and non-interference with the natural process of labor should be adopted by every obstetrician and physician practicing obstetrics, a great step will have been taken in reducing the number of maternal and fetal deaths and maternal morbidity.

From the beginning, our policy has been one of "watchful waiting and non-interference", except for absolutely definite indications. It has been our principle to give the parturient a chance, for, after all, nature has endowed woman with the necessary powers of accommodating herself to the various conditions which may arise during labor; and, after one thousand women have been delivered by following such a policy of conservatism, we are firmly reassured and justified in our belief and principle, that, "watchful waiting and non-interference", except for absolutely definite indications, is the best policy to follow in the interest of both mother and child. During this period we stuck to our principle patiently, conscientiously, and judiciously, interfering only for an absolutely necessary indication, regardless of the lateness of the hour, the interference with our sleep, or the keeping of professional or social engagements. No interference was undertaken solely to save time, or to quiet the importunities of either the patient or the patient's family. It has been a source of much satisfaction that in the end we were rewarded in our judgment with good results for both mother and newborn, and with the knowledge that we had not, through any haste or laxity, errors of omission or commission, or undue interference, been responsible for the very little maternal morbidity and infant mortality that we were unfortunate enough to

*Read before the Massachusetts Italian Medical Society.

†Macchia, Bart F.—For record and address of author see "This Week's Issue," page 285.

have had, during this period. Our consciences were clear and we could not reproach ourselves for any unfortunate outcome.

In the series on which this paper is based, one thousand women were delivered of one thousand and fifteen infants. These were delivered from January, 1925 to March, 1932, and with the exception of a very few were delivered at home and under conditions which one meets among the poorer classes of patients.

It can be realized that even in a short series of one thousand cases, one can show some proof that the most important causes of maternal morbidity, fetal injuries, and fetal and maternal mortalities are the following:

1. Premature and unnecessary interference.
2. Eagerness on the part of the busy practitioner to get over the case as soon as possible.
3. Lack of proper training of the obstetrical attendant (a) to determine the proper time to interfere with the normal and natural process of labor, and (b) to employ the proper operation in a given case.
4. To the "Furor Operativus" of some obstetricians.
5. And last but not least, and also shameful to relate, to the "Furor Dollaritis" of a few unscrupulous physicians, who undertake operative deliveries with no indication whatever, except that they may enrich themselves to the extent of a few dollars.

Of these one thousand cases, only nine were delivered at hospitals; the remainder were home deliveries. There were two hundred and thirty-four primiparas and seven hundred and sixty-six multiparas. The positions and presentations at the beginning of labor or when first seen in labor were as shown in chart I.

CHART I

	No.	Delivery Normal	Operative
Left Occiput Anterior	678	653	25
" " Posterior	5	3	2
Right " Anterior	49	47	2
" " Posterior	182	170	12
Left " Transverse	7	4	3
Right " "	22	20	2
Vertex and hand	3	2	1
Left, Brow Anterior	2	2	—
Face (1 chin posterior)	6	3	3
Breech {frank 24 - complete; Single 6 Footling 10}	40	40	—
Transverse (Torso presentation	6	—	6
Total	1000	944	56

NOTE: Only the first of twins was considered in the above in order to simplify calculations of percentages.

In this series of representative cases, both as regards varieties of presentations, and positions as well as all types of patients, and not as a selected group, but as the usual run of cases with which one is confronted in the everyday practice of obstetrics, nine hundred and forty-four were delivered normally and only fifty-six were delivered by operation; an operative incidence of 5.6 per cent. Of these fifty-six operations;

Low Forceps was performed 12 times.
Mid Forceps was performed 15 times.
High Forceps was performed 2 times.
Scanzoni (DeLee modif.) was performed 2 times.
Version was performed 23 times.
Caesarian was performed 2 times.

From the very low operative incidence, and particularly from the small number of Caesarians, one would be apt to come to the conclusion that this series was from a selected group. On the contrary, we assure you that this was not a picked group of cases, but the usual run, and, as has been stated, the first thousand in our practice of obstetrics. Many of these patients were not seen prenatally, nor had they received prenatal care elsewhere, nor are they cases from a race of people endowed with superior physical or generative powers.

In a prolonged labor, when the condition of the mother and child was good, regardless of the patient's pleadings, or the implorations of the family to, "Do something, Doctor," we bided our time, relieving the patient's sufferings with various analgesics, of which we have used morphine gr. 1/6 and scopolamine gr. 1/150-1/200, sodium amytal grs. 6-9 alone or proceeded with an injection of morphine, and also the so-called Gwathmey analgesia, which in substance is an injection of morphine gr. 1/4 in a solution of 25 per cent magnesium sulphate, followed in time with an administration of an ether-oil mixture per rectum. These have been followed by good results, preserving the patient's strength and mental attitude. Operation was resorted to only for definite indications and in the interest of mother and child.

When we were confronted with a case where we felt that interference was justified, we deliberated carefully on the choice of operation, and decided on the one which would give the best results, taking into consideration both mother and child. The indications for which these were performed were as follows:

Low Forceps

Inertia—3, cardiac disease—2, dystocia—5, fetal distress—1, eclampsia—1.

Mid Forceps

Inertia—6, dystocia—2, stemmed at ischial spines—7.

Scanzoni (DeLee modification)—

Persistent occiput posterior position—2.

High Forceps

Disproportion—failure of head to engage after an adequate test of labor—potentially infected cases—2.

Version

Persistent posterior occiput position—4, inertia—2, transverse (torso presentations)—7, placenta previa—2, prolapsed cord—4, face presentation—1, chin posterior—1, fetal distress—1, second of twins—1.

Caesarian

Abruptio placenta—1, disproportion—1 (previous section).

Caesarian section was performed in only two instances, this in spite of the fact that many obstetricians report as high as 10 to 15 per cent incidence.

The operative frequency and mortality for each procedure, together with the normal deliveries in this series, were as follows:

In the normal deliveries the 14 neonatal deaths were the following: 4 nonviable premature, 2 due to asphyxia neonatorum, 2 due to inanition, 1 to hemorrhage from the cord with resulting anemia, 1 to pemphigus neonatorum, 1 had congenital heart, 1 congenital obstruction of the sigmoid, 1 congenital obstruction of the anus and 1 was an anencephalous monster. Of the 16 stillbirths in the normal deliveries 8 were macerated, 2 were the result of intrauterine asphyxia due to premature separation of the placenta, 1 was an anencephalus, 1 a hydrocephalus, 1 a spina bifida, 1 had a true knot in cord with three loops around the neck, and in two instances the causes were not determined.

Occiput Posterior Positions. Of the 946 vertex presentations, the occiput posterior position occurred 187 times, an incidence of 18.7 per cent. (R.O.P.—182 and L.O.P.—5.) Spontaneous rotation of the occiput took place in

CHART II

Method of Delivery	No.	Per cent Frequency	Maternal Deaths	Fetal Deaths	
				Neonatal	Stillborn
Low Forceps	12	1.2	0	0	0
Mid Forceps	15	1.5	0	1	1
High Forceps	2	.2	0	1	0
Scanzoni (DeLee mod.)	2	.2	0	0	0
Version	23	2.3	0	1	6
Caesarian Section	2	.2	0	0	1
Normal Deliveries	944	94.4	0	14	16
Total	1000	100	0	17	24

In the whole series there was an uncorrected fetal mortality of 4.1 per cent. The corrected fetal mortality, after subtracting the unavoidable deaths, which consisted of seven nonviable premature infants, nine macerated fetuses, two anencephalous monsters, one hydrocephalus, one spina bifida, two with congenital obstruction of anus and sigmoid and one with a congenital heart, was 1.8 per cent.

The highest incidence in fetal mortality occurred in the operation of version. Of course this high mortality can be easily understood, for version was performed for serious indications, as a glance at indications shows. Of the seven fetal deaths, 1 neonatal and 6 stillborn, the causes were as follows: prolapsed cord in two instances, placenta previa with bleeding, two instances, intrauterine distress and asphyxia, two instances, and premature with cord knotted and two loops around neck in one instance.

Of the two deaths occurring in mid forceps operations, 1 neonatal was due to prolonged labor with intrauterine distress and asphyxia, and the other was a macerated stillborn.

The neonatal death in high forceps was due to birth injury.

The stillbirth in the Caesarian section was due to ablatio placenta.

163 cases or about 87 per cent of the occiput posterior positions. The occiput rotated to the sacrum in nine instances, or in a little less than 5 per cent of the cases. Seven of the latter were delivered spontaneously and two were delivered in that position by forceps.

We believe in letting posterior occiput positions rotating to sacrum alone, or in delivering them by forceps in that position; because attempts to rotate them anteriorly are attended with considerable danger to both mother and child.

Persistent occiput posterior positions requiring interference occurred 15 times, or in 8 per cent of the posterior positions. Of these 15 cases of persistent posterior positions, 3 were rotated manually and later delivered normally, 4 were manual rotations followed by forceps applications and delivery, 4 were delivered by internal podalic version, 2 delivered in that position by forceps and 2 by the DeLee modification of the Scanzoni-Tarnier-Bill maneuver.

Breech. The breech presentation occurred in 40 instances, or in 4 per cent of all deliveries: frank breech 24 times, single breech 6 times and footling 16 times. It occurred in primiparas 14 times and in multiparas on 26 occasions.

Our treatment of such cases was very con-

servative, assisting the normal process, and not attempting to extract the fetus prematurely. There were 8 fetal deaths; 3 were macerated, 2 were nonviable premature fetuses and 3 can be attributed to the extraction. This gives a corrected fetal mortality of 7.5 per cent for breech deliveries. All three of these deaths occurred in primiparas with babies larger than normal.

Transverse presentations wherein some part of the infant's torso presented, were found on six occasions in women in labor and in one case before labor had set in. Those in labor were all treated by podalic version. With the one case not in labor, an external conversion to vertex was accomplished and she was later delivered normally in R.O.A. Only one fetal death occurred in these cases; this was due to asphyxia.

Face presentations occurred on six occasions. In one of these the chin was posterior, in the sacrum. The instance of chin in the hollow of the sacrum and one of the others of face presentations were delivered by version, two others normally in that position, one converted to brow and delivered by low forceps and the other converted to L.O.A. and delivered normally.

Brow. The two brow presentations were delivered normally; in that position, on one occasion, and after conversion to vertex on the other.

Vertex and hand presentation, wherein the hand was prolapsed in the vagina and presented with the vertex, was found on three occasions. In two instances the hand was replaced and delivery allowed to take place normally, and in one case a version was performed after failure of hand to remain permanently replaced.

Occiput transverse presentations, of which there were 29—R.O.T.—22, L.O.T.—7, 5 were delivered by forceps.

Pituitrin. In sixty-seven deliveries the use of pituitrin, never more than 0.5 cc, was resorted to in cases of partial or total uterine inertia, only when the head (that is its greatest circumference) had passed the line joining the ischial spines, the cervix fully dilated and its lower uterine portion taken up, the absence of a Bandl's ring, and the membranes ruptured, with no unpleasant results or ill-effects to either mother or child. On the contrary, we feel that the careful and judicious use of pituitrin in such cases was an advantage; for, in a great number of these cases, forceps would have had to be used with consequent injuries to both mother and child. Of course we do not recommend the use of pituitrin, unless as stated above, with conditions ideal and only when the safety of the mother or child makes immediate delivery necessary. There was one fetal death in this series, due to asphyxiation, but we feel that this was not caused by the use of pituitrin. This occurred in a primipara with uterine inertia, the fetal heart showing signs of distress, the vertex visible at the introitus. Pituitrin 0.5 cc. was given and an episiotomy was performed, so that the head would have free unimpeded exit.

Lacerations. There were forty-seven lacerations of the perineum or introitus. Thirty-seven occurred in primiparas and ten in multiparas. Thirty were first degree, fifteen second degree and two were third degree tears. Of the first degree tears, twenty-three occurred in primiparas and seven in multiparas, of which three of the latter were after forceps deliveries and the remainder after normal deliveries. Of the second degree tears, 14 occurred in primiparas and 1 in a multipara. Six of the second degree tears occurred after forceps deliveries. The two third degree tears occurred in multiparas. One, in reality, was a separation of a thin septum of scarred tissue between the vagina and rectum of a woman who had had a complete tear at her first delivery four years previously, and who had had no control of her sphincters since that time. Incidentally a perineorrhaphy was done in this case at the time of delivery with good results as to the control of the sphincters, and fairly good anatomical results, in spite of the existing atrophy of the structures. The other tear was caused by a too rapid expulsion of the shoulders of a large baby of a secundipara, whose vulval tissues seemed to be as friable as wet blotting paper. We had taken a great deal of care in the delivery of the head without tearing, only to have the misfortune of the patient's making a vigorous expulsive effort with the after-coming shoulders.

There were three cervical tears in this series that required suturing. All occurred in primiparas after forceps deliveries.

We ascribe this very low incidence of lacerations to our practice of ironing out the perineum, protecting the perineum and the slow delivery of the head in an oblique position at the vulval outlet. This practice in full consists of (1) ironing out the perineum; (2) keeping the head well flexed; (3) delivering the head very slowly; and (4) allowing the head, that is the suboccipital-bregmatic, suboccipital-frontal and suboccipital-mental diameters, to successively slip over the vulva in a slightly oblique position. The ironing out of the perineum is of course undertaken in the usual manner, under strict aseptic precautions and with the use of green soap for lubrication.

Episiotomy. This procedure was practiced in only 13 cases, showing a decidedly conservative tendency. It was performed on 12 primiparas and on 1 multipara; in normal deliveries on 5 occasions and in forceps operations on 8 occasions.

The low incidence of lacerations that we have encountered, and the success that we have

had in preventing perineal tears, by the method of protecting the perineum and the delivery of the head, have made us reserve the performance of episiotomy for cases where a rapid delivery in the interest of the mother or child is necessary. Furthermore, we have found that a laceration, properly sutured and cared for, will give as good results, and do not believe in brutally and intentionally inflicting a wound to an already suffering parturient.

Complications intercurrent with labor. We delivered six mothers who had serious organic heart conditions and three with pulmonary tuberculosis, without any bad after-effects. Three women had chronic kidney ailments and delivered normally and safely, and one had eclampsia with convulsions while in labor. The latter was delivered by forceps, the convulsions stopping after delivery. Two women had influenza, three had pyelitis and one had an acute bronchitis.

Three parturients who had had a previous Caesarian were delivered by the vaginal route. On one of these, a classical Caesarian had been done four years previously, and she had had such a stormy convalescence that she absolutely refused to undergo another Caesarian. This woman was allowed to go into labor and then delivered by an easy mid forceps operation. Subsequently, she was delivered on three other occasions normally, the smallest infant weighing eight and three-quarters pounds, the largest twelve pounds. The primipara, who had an ablatio placenta in this series and on which a section was done, was delivered three years later by mid forceps. The other case was a premature delivery at six months.

Morbidity. As regards morbidity, we shall not undertake to give an estimation, because it is impracticable to do so, unless all parturients are followed up for a number of years after labor. One can readily understand the impossibility of such an undertaking if one can visualize and take into consideration the late inevitable consequences of pregnancy and labor. Therefore, we shall enumerate only the incidence of temperature of 100.4 degrees or over of more than forty-eight hours' duration and those conditions which came under our observation during the puerperium.

There were 26 patients with fever of 100.4 and over for more than 48 hours. Of these 26 cases, the fever was accounted for by infection of perineal lacerations—4 cases, pelvic infection in 3 instances, systemic sepsis—1, phlebitis—2, pyelitis—3, mastitis and breast abscesses—4, acute upper respiratory infections in 3 instances, pulmonary tuberculosis—1, and in 5 instances the cause was undetermined.

There were four instances of antepartum hemorrhage; two from placenta previa, one partial premature separation of a low implanted placenta and one from partial separation of a normal implanted placenta.

There were seventeen instances of postpartum hemorrhage. Eleven were due to atony of uterus, two to retained placental fragments or membranes, three to cervical tears, and in one instance the patient was a bleeder. The cases of atony of uterus were easily controlled by pituitrin, ergot and massage. There were no instances of retained placenta that required invasion of the uterus and manual removal. Those that did not deliver spontaneously, were "Credéd."

The following abnormalities, congenital malformations and monsters were delivered in this series: anencephalus—2, hydrocephalus—1, spina bifida—1, cleft palate—1, hare lip—1, equino varus—2, congenital obstruction of sigmoid—1, imperforate anus—1, epispadias—1; one child had one normal eye; on the other side there was a socket but no eyeball. This child also had a torticollis on the defective side due to underdeveloped cervical muscles. One infant had a congenital heart.

Fifteen pairs of twins were delivered in this series of one thousand cases, making a total of one thousand and fifteen newborn. Nine pairs were of the same sex; seven pairs of females and two pairs of males and six pairs were mixed sexes. One of the twins, the second, succumbed to asphyxiation due to separation of the single common placenta.

CONCLUSIONS

In conclusion, we wish to state that the appalling maternal morbidity and maternal and fetal mortality that occur in this country are, in a large measure, due to (1.) "Furor operativus" of some obstetricians. (2.) Unnecessary interference with the normal and natural process of labor. (3.) Lack of proper training of the obstetrical attendant in, (a) failure to recognize the proper time for interference, (b) failure to choose the proper method of delivery.

That labor, in about 95 per cent of the cases, is a natural and normal process, and should be regarded as such.

That the duty of the obstetrical attendant should at all times be in the nature of protecting the parturient from injury, and assisting and not interfering with the normal process of nature and labor.

That it can be seen by this series of cases that 94.4 per cent of parturients can be and were delivered normally.

That only 2.6 per cent of the parturients suffered any immediate morbidity, and only 4.7 per cent had lacerations of the perinéum.

That there were no maternal deaths and a corrected fetal mortality of 1.8 per cent.

That laceration of the perineum can be prevented to some extent by the proper preparation and protection of the perineum, and the careful delivery of the child's head.

That the use of pituitrin in small quantities is a safe undertaking, and has its advantages when used judiciously and under proper conditions.

That 87 per cent of occiput posterior positions will rotate to the anterior position if given a chance, and that about 90 per cent of all posterior positions will deliver spontaneously if left to nature.

And finally, that "watchful waiting and judicious interference" equals less morbidity and less mortality.

MORTALITY RATES

Telegraphic returns from 86 cities, with a total population of thirty-seven millions for the week ending July 21, indicate a mortality rate of 10.2 as against a rate of 9.5 for the corresponding week of last year. The highest rate (21.5) appears for Kansas City, Mo., and the lowest (4.7) for Flint, Mich. The highest infant mortality rate (17.0) appears for Hartford, Conn., and the lowest for Albany, N. Y., Dayton, Ohio, Louisville, Ky., South Bend, Ind., Trenton, N. J., and Yonkers, N. Y., which reported no infant mortality.

The annual rate for 86 cities is 11.9 for the twenty-nine weeks of 1934, as against a rate of 11.3 for the corresponding period of the previous year.

SUMMARY OF DEATHS AND DEATH RATES (ANNUAL BASIS) FROM AUTOMOBILE ACCIDENTS PER 100,000 ESTIMATED POPULATION FOR 86 CITIES FOR CORRESPONDING PERIODS OF 1934 AND 1933

	Week ending		First 29 weeks	
	July 21, 1934	July 22, 1933	1934	1933
Total deaths	135	144	4,523	4,006
Death rate	18.8	20.1	21.7	19.2
Deaths due to accidents in city	101	110	3,629	3,184
Death rate	14.1	15.3	17.4	15.3

—*Bureau of the Census.*

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1934

Typhoid fever and diphtheria had their lowest reported June morbidity.

Anterior poliomyelitis is following its usual trend to date.

The incidence of dog bites continues high.

Pulmonary tuberculosis remains lower than the five-year average although slightly higher than June, 1933.

Chicken pox, whooping cough, and measles are somewhat more prevalent than usual for the month.

Lobar pneumonia, scarlet fever, mumps, tuberculosis other forms, German measles, and epidemic cerebrospinal meningitis show nothing remarkable.

RARE DISEASES

Anterior poliomyelitis was reported from Framingham, 1; Haverhill, 1; Newton, 1; Orange, 1; total, 4.

Dysentery (amebic) was reported from Malden, 1; Medford, 1; Southbridge, 1; Worcester, 4; total, 7.

Dysentery (bacillary) was reported from Boston, 1; Danvers, 11; total, 12.

Encephalitis lethargica was reported from Greenfield, 1; total, 1.

Epidemic cerebrospinal meningitis was reported from Falmouth, 1; South Hadley, 1; Springfield, 2; Weymouth, 1; total, 5.

Leprosy was reported from Westfield, 1; total, 1.

Malaria was reported from West Stockbridge, 1; total, 1.

Pellagra was reported from Swampscott, 1; total, 1.

Rabies was reported from Lynn, 1; Winthrop, 1; total, 2.

Septic sore throat was reported from Amesbury, 1; Boston, 9; Brookline, 1; Cambridge, 1; Everett, 1; Framingham, 1; Lowell, 4; Mansfield, 2; Medford, 1; Watertown, 1; total, 22.

Tetanus was reported from Great Barrington, 1; total, 1.

Trachoma was reported from Boston, 2; Everett, 1; Quincy, 1; Westwood, 1; total, 5.

Trichinosis was reported from Boston, 1; total, 1.

Undulant fever was reported from Richmond, 1; Stoneham, 1; total, 2.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

MONTHLY REPORT FOR JUNE, 1934

Disease	June, 1934	June, 1933	Average*
Anterior Poliomyelitis	4	3	6
Chicken Pox	1150	1006	979
Diphtheria	41	81	178
Dog Bite	1262	803	738
Epidemic Cerebrospinal Meningitis	5	1	11
German Measles	92	85	289
Gonorrhea	566	655	562
Lobar Pneumonia	242	189	213
Measles	3382	2419	3005
Mumps	467	534	599
Scarlet Fever	732	1018	913
Syphilis	426	439	331
Tuberculosis Pulmonary	348	317	366
Tuberculosis Other Forms	41	38	52
Typhoid Fever	4	8	16
Undulant Fever	2	2	—
Whooping Cough	970	715	680

*Average number of cases for June during the preceding five years.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 20321

The patient was a sixty-five year old American collector. During the past ten years he had had an occasional feeling of discomfort in his epigastrium after meals, but no marked symptoms. One year before admission he began to have some dyspnea upon climbing stairs, but considered himself in fairly good condition. Ten days before entry he had a sudden attack of epigastric and precordial discomfort while in bed at ten p. m. He had felt well at supper and had taken a hot bath before going to bed. The epigastric pain was that of an intense pressure. He lay awake in bed fearful. At two a. m. he began to have pain in the left axilla and left arm extending to the elbow. He remained awake all night. In the morning his physician gave him some pills which relieved the arm pain but not the epigastric discomfort. He stayed in bed for four days feeling weak and out of breath. He remained at home for a few more days, still dyspneic but up and about. Four days before entry he went to his office and felt somewhat better. The evening before entry, after making several calls, he felt exhausted and dyspneic.

His mother died of cancer, his father of a stroke.

The patient was a bachelor and lived alone in a rooming house.

His past history is irrelevant except for slight failing vision.

Physical examination showed a sick looking middle-aged man in moderate respiratory distress. The fundi showed moderate sclerosis of the arteries. The skin and mucous membranes were moderately pale and there was slight cyanosis of the lips. The chest was moderately barrel shaped and the expansion was somewhat limited. The heart was moderately enlarged to the left, the apex being 11.5 centimeters from the midsternal line in the fifth interspace. The sounds were of poor quality. The second sound was reduplicated at the apex. There was a faint systolic murmur at the apex. The blood pressure was 128/92. There was some dullness at both bases, with medium coarse moist râles to the midscapular region and a few moist râles anteriorly. There was dullness, resistance and some tenderness three or four fingerbreadths down in the right costal margin. There was slight pitting edema of the ankles and shins.

The temperature was 99.7°, the pulse 100. The respirations were 27.

Examination of the urine was negative. Examination of the blood showed a red cell count of 4,500,000, a hemoglobin of 80 per cent. The white cell count was 13,400, with 91 per cent polymorphonuclears. The Hinton test was negative. The non-protein nitrogen was 33 milligrams. The icteric index was 5.

X-ray examination showed marked increase of the heart shadow both to right and left of the spine, with obliteration of the right cardiohepatic angle and increase in the supracardiac shadow. The transverse diameter of the heart was 15.8 centimeters, 10.5 centimeters to the left and 5.3 centimeters to the right. The transverse diameter of the chest was 28 centimeters. The hilus shadows showed marked increase both in width and density. Both costophrenic angles were obliterated by dull areas which extended upward in the axillary lines.

He was put on complete bed rest, soft diet, fluids up to 70 ounces and morphia grains 1/6 every three hours p.r.n. He developed Cheyne-Stokes breathing and became very cyanotic. On the second day his chest was filled with râles. An electrocardiogram showed a high take-off of T waves. On the third day he became very unresponsive and more cyanotic, and in spite of being in an oxygen tent rapidly failed and died.

DIFFERENTIAL DIAGNOSIS

DR. J. H. MEANS: On the face of it this would seem a very simple diagnostic problem.

The ten years of occasional epigastric discomfort after meals may or may not be significant. Without more information than we have, I would not be willing to evaluate it.

The dyspnea beginning a year ago certainly is of importance in view of subsequent developments. It probably denoted the beginning of diminishing cardiac reserve, or it may have been a result of increasing emphysema. The sudden attack of ten days before entry was fairly typical of acute coronary occlusion, i.e., sudden epigastric and precordial pain while in bed with sensation of pressure with later radiation to the left arm and axilla. Dyspnea lasting four days, even in bed, followed. I cannot square this with simple angina pectoris, which does not come on, at least for the first time, when a patient is in bed, nor is it followed by four days of impressive dyspnea, nor does it last several hours.

One thinks of other acute cardiovascular episodes which may resemble coronary occlusion. One is pulmonary embolism. Sometimes this gives symptoms almost identical with coronary occlusion; so also sometimes does dissecting aneurysm of the aorta. I cannot believe, however, that he would have been out of bed and able to be about in four days if either of these had happened to him.

The symptoms which immediately led to hospitalization seem to have been weakness and dyspnea, and his physical examination showed evidence of arteriosclerosis, emphysema, large heart, pulmonary edema, probably engorged liver, and slight edema of the ankles; in other words, the picture of beginning congestive failure. Slight leukocytosis and temperature could be either the aftermath of a coronary thrombosis ten days before or merely manifestations of cardiac decompensation.

We should like to know what his usual blood pressure had been to determine whether there had been a drop, as there usually is in coronary occlusion. His kidneys apparently were good.

The x-ray examination adds but little to what we already know,—big heart, increased hilus shadows probably due to pulmonary congestion, edema of the lung bases and perhaps some bilateral hydrothorax. The obliteration of the cardiohepatic angle suggests pericardial effusion, but could also be due to simple big heart. The cardiogram is consistent with cardiac infarct.

The possibility that the whole acute affair is pericardial occurs to one. It impresses me as a highly unlikely explanation. If one knew that there was a pericardial friction rub, one would be even more firmly convinced that the heart had been infarcted. Even without that sign, I believe the chances strongly favor that diagnosis. Indeed, my expectation is that the pathologist will find:

Generalized arteriosclerosis.
Cardiac hypertrophy, bilateral.
Left sided, due to hypertension which I believe probably once existed.
Right sided, due to pulmonary emphysema.
Coronary thrombosis and
Cardiac infarction.
Probably visceral pericarditis caused by infarct, and perhaps some pericardial effusion.
Congestion of both lungs.
Perhaps bilateral hydrothorax.
Emphysema.
Congestion of the liver.

The immediate cause of death is cardiac failure.

I should like to add my criticism of the treatment. It certainly seems to me that this man should not have been allowed up in four days. Whether he had coronary thrombosis or not, he at least had a good imitation of it, and this alone was absolute indication for six weeks or more of complete bed rest. Had he been kept in bed, he might have survived.

Clinical Diagnoses

Coronary thrombosis.
Congestive heart failure.

Anatomic Diagnoses

Coronary thrombosis, left interventricular.
Myocardial infarct.
Pericarditis, acute fibrinous.
Hydrothorax, bilateral.
Arteriosclerosis, moderate coronary and aortic, slight renal.
Medionecrosis aortica cystica, very slight.
Rupture of descending aorta, very slight.

Pathologic Discussion

Dr. Tracy B. Mallory: As Dr. Means predicted, we found a thrombosis of the descending branch of the left coronary artery. We felt that an older organized portion and a fresh recent one could be distinguished, the fresh lesion only a few days old, the organized one dating back at least several months. Consequent to the last thrombus, infarction of the apex of the left ventricle and of a portion of the interventricular septum had developed. The pericardium showed not merely the few shreds of fibrin that are almost invariably found over a fresh infarct but a relatively massive fibrinous exudate of the type often described as "a bread-and-butter heart". On the ventricular surface of the infarct a mural thrombus had formed.

The possibility of a dissecting aneurysm which Dr. Means mentioned was actually not far from the truth. We did find the beginnings of such an aneurysm with a small rent in the intima and a very short zone of distention. Sections from other parts of the aorta showed small cystic spaces in the media—the idiopathic cystic aortitis of Erdheim—which is actually the most frequent precursor of dissecting aneurysms. If his coronary occlusion and myocardial infarction had not killed him when they did, I believe that in a few days or weeks he would have died from a dissecting aneurysm.

The other findings in the case were simply diffuse arteriosclerosis and chronic passive congestion.

CASE 20322

Presentation of Case

The patient was a fourteen months old colored boy who was admitted at two a. m. with a severe cough and respiratory difficulty.

The child's delivery was normal, at term. He was breast fed for six months and then given diluted milk. Cod liver oil and orange juice were started at three months, vegetables at five months and cereals at six months. His development was normal. He had been perfectly well until the present illness.

The family history was essentially negative except that an older brother had a cold at the time of the patient's admission, but was not whooping.

The child had had a severe cough beginning with a running nose three weeks before admission. The cough had increased in severity and was present more during the night than during the day. For the past week there had been a definite whoop. The child had been vomiting after his meals, but had seemed in good condition until the day before admission, when he developed a fever and seemed to be breathing with difficulty. The night of admission the parents had taken him to two hospitals, where he had been refused admission.

Physical examination showed a well-developed and nourished colored boy who was acutely ill but quite coöperative. His temperature was 104.6°, respiration 48, and pulse 164. He had definite paroxysms of coughing. The respirations were rapid and short. The throat was red. There was a mucopurulent nasal discharge. The lungs showed generalized impairment of resonance. Moist and subcrepitant râles were present. The heart was enlarged; the rate was rapid and the sounds were of good quality; no murmurs were heard. The abdomen was distended.

Laboratory work. The white blood cell count was 150,000; a second count 190,000. The differential count showed 32 per cent polymorphonuclears, 68 per cent lymphocytes, no monocytes, eosinophils or basophils.

Because of his condition the child was admitted to an isolation room in the Emergency Ward. At five o'clock that morning there was a definite change for the worse. He was put on the danger list at 6.40. He was toxic and unresponsive. The pulse rate was 160 and weak. The respirations were rapid and Cheynes-Stokes in type. His temperature was 107.6°. He was placed in an oxygen tent. The respirations became more apneic. There were twitchings on one side of the body. The oxygen afforded little relief. The spinal fluid was slightly turbid. Of 680 cells 12 per cent were polymorphonuclears and 88 per cent lymphocytes. No organisms were seen in the Gram stain. Tests for globulin were positive.

The baby died at 9.41 the morning of admission.

Differential Diagnosis

Dr. Harold L. Higgins: This patient seems pretty definitely to have whooping cough and to demonstrate some rather characteristic and some rather disturbing symptoms of the disease.

The child is fourteen months old, an age when whooping cough is a very serious illness. The younger a child is the more serious it is. In children under six months of age the fatality may run as high as fifty per cent. The death rate gradually diminishes as children get older.

This child was having the usual course of whooping cough until the day before admission, when he had fever and difficult breathing. That seems to mark the onset of bronchopneumonia, and the more so because he was toxic.

This child being in the third week of the disease still was contagious, and one does not blame a hospital for refusing to accept him. It does seem, however, as if they should have realized how sick he was and should have referred him to a hospital that would have accepted him. We admitted him because he was so sick. We put him in a room by himself where he would not give the disease to other children.

He had a mucopurulent nasal discharge. It does not seem to be generally known that whooping cough usually starts as a rhinitis, an ordinary cold. Then it develops into a pharyngitis and finally into a bronchitis. In the ordinary cold, however, the child coughs for a few days, then the cough gets better, except that it may become marked at night. The night cough is characteristic of the ordinary cold and is caused by mucus going down the wrong way as the child lapses into sleep. In the daytime the child swallows the mucus; at night it enters the larynx. With whooping cough, however, the patient coughs day and night at almost regular intervals.

The heart was enlarged; apparently a dilatation.

The story of the difficult breathing and toxicity perhaps leads to a toxic meningitis.

The white cell count in this case is perhaps quite startling to one who has not seen many cases of whooping cough. There is a white cell count of 150,000 and a later count of 190,000. High white cell counts are frequently found in whooping cough pneumonia. I recall one patient with a count of 252,000. The differential count in these cases of whooping cough pneumonia is usually about half lymphocytes and half polymorphonuclear neutrophils; the lymphocytes are high because of the whooping cough and the polymorphonuclears on account of the pneumonia. There were so many lymphocytes and so many polymorphonuclears that no monocytes were found in the count.

This very sick child began to show some rather unusual symptoms. He is described as being comatose and developing Cheyne-Stokes breathing. Cheyne-Stokes breathing is a definite indication of something wrong around the respiratory center of the brain, a medullary involvement. His temperature went up to 107.6°, another indication of something wrong in the medulla. The child was put in an oxygen tent, but it did not relieve him to any great extent. There were twitchings on one side of the body, a sign of cerebral involvement. A lumbar puncture was done and a slightly cloudy fluid withdrawn with 680 cells and 88 per cent lymphocytes. There was globulin present, but no organisms were found.

My diagnosis is whooping cough with second-

ary bronchopneumonia and some cerebral involvement. It does not seem to be a secondary purulent meningitis because there is such a low percentage of polymorphonuclears. The 88 per cent lymphocytes makes me feel that perhaps this is a manifestation of a whooping cough encephalitis. Whooping cough will in some cases lead to encephalitis. It is not a very rare complication of whooping cough. Following the whooping cough an occasional child has become mentally retarded. We used to ascribe this mental retardation from whooping cough to cerebral hemorrhage caused by violent coughing; but recent investigation has shown pretty clearly that it is an encephalitis from some virus or toxin associated with the whooping cough injuring or destroying the brain cells. I expect the necropsy in this case to show signs of encephalitis.

I do not believe it is a secondary meningitis, although one certainly has to think of tuberculous meningitis here. Our data in regard to tuberculosis are not very complete.

Clinical Diagnosis

Pertussis.

Anatomic Diagnoses

Interstitial pneumonia.
Acute bronchitis.
Cerebral edema.
"Toxic encephalitis."

Pathologic Discussion

Dr. Tracy B. Mallory: The autopsy here showed a marked bronchitis, but no evident areas of consolidation in the lungs.

The brain showed a slight increase in the amount of subarachnoid fluid, but in gross it was impossible to make a diagnosis of meningitis. Cultures from both the blood and the spinal fluid were negative.

Microscopic examination showed us a little more. The lungs showed in the smaller bronchi and bronchioles a uniform infiltration of the walls with mononuclear cells, lymphocytes, plasma cells and large mononuclears in varying but roughly equal proportions. This process seemed to extend over from the bronchioles to the immediately contiguous alveoli, but there were no large areas of pneumonia. In the alveoli the great majority of the cells were large mononuclears rather than polymorphonuclears, and there was no fibrin present. This distribution of an acute infectious lesion corresponds to what is now being called interstitial pneumonia, which Rich and various others believe is characteristic of virus pneumonia. It is found in whooping cough, in measles and in the early uncomplicated stages of influenza, possibly in some other diseases. In addition the question is being hotly argued at the present time as to whether these cases of pertussis show inclusion bodies in the cells. They are reported pretty regularly by McCordak in St. Louis. Rich doubts their significance. We looked very carefully for inclusion bodies here, but could not find any that I was confident about.

The brain showed a similar exudate in the meninges, a combination of mononuclears and polymorphonuclears, the mononuclears predominating. Within the brain there was a great deal of degeneration of ganglion cells shown by Nissl stains, but no evidence of an inflammatory process within the brain, though encephalitis ought to show inflammatory lesions within the brain substance. Perhaps that is quibbling on a technical point. What was found is very close to what has been described in cases of so-called pertussis encephalitis.

A Surgeon: What is the present viewpoint in regard to the etiology?

Dr. Mallory: The shift is very strongly in favor of this being a primary virus disease. Positive evidence however is lacking. The inferential evidence from the frequency of interstitial pneumonia and the frequency of encephalitis is pretty good. The Bordet-Gengou bacillus is still found with considerable regularity, almost uniformly. I think a positive Bordet-Gengou isolated from the sputum is still considered very reliable diagnostic evidence. Is that not so, Dr. Higgins?

Dr. Higgins: Yes.

Dr. Mallory: It is quite possible that the relationship to the disease is like that of virus and bacillus in swine influenza. The association is almost one hundred per cent. It is rather improbable, however, that the bacillus alone could initiate the disease.

The New England
Journal of Medicine

SUCCESSOR TO
THE BOSTON MEDICAL AND SURGICAL JOURNAL

Established in 1828

Published by THE MASSACHUSETTS MEDICAL SOCIETY under the jurisdiction of the

COMMITTEE ON PUBLICATIONS

R. I. Lee, M.D., *Chairman* HOMER GAGE, M.D.
R. B. OSGOOD, M.D. R. M. SMITH. M.D.
F. H. LAHEY, M.D.

EDITORIAL STAFF

REID HUNT, M.D. STEPHEN RUSHMORE, M.D.
JOHN P. SUTHERLAND, M.D. HANS ZINSSER, M.D.
GEORGE R. MINOT. M.D. BENJAMIN WHITE, PH.D.
FRANK H. LAHEY, M.D. HENRY R. VIETS, M.D.
SHIELDS WARREN, M.D. ROBERT N. NYE, M.D.
GEORGE L. TOBEY, JR., M.D. ROBERT M. GREEN, M.D.
C. GUY LANE, M.D. CHARLES C. LUND, M.D.
WILLIAM A. ROGERS, M.D.

WALTER P. BOWERS, M.D., *Managing Editor*

ASSOCIATE EDITORS

GEORGE G. SMITH, M.D. WILLIAM B. BREED, M.D.
JOSEPH GARLAND, M.D.

THE NEW HAMPSHIRE MEDICAL SOCIETY
PUBLICATION COMMITTEE

CARLETON R. METCALF HENRY H. AMSDEN
WARREN H. BUTTERFIELD

THE VERMONT STATE MEDICAL SOCIETY
PUBLICATION COMMITTEE

WILLIAM G. RICKER, M.D. C. F. DALTON, M.D.
E. A. STANLEY, M.D.

SUBSCRIPTION TERMS: *$6.00 per year in advance, postage paid for the United States, Canada $7.04 per year, $8.52 per year for all foreign countries belonging to the Postal Union.*

Material for early publication should be received not later than noon on Saturday. Orders for reprints must be sent to the Journal office, 8 The Fenway.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to The New England Journal of Medicine, 8 The Fenway, Boston, Mass.

EDUCATION IN MEDICINE AND IN LAW

IT is natural for the physician to think that the general practice of medicine requires a more extended educational preparation than does the general practice of law. Is this opinion justifiable?

It is not claimed that the law does not offer opportunity for gifts of the highest type. It does this as truly as does medicine. But the field of novelty in medicine is far greater than in law. In a very real sense no two cases in medicine are alike: the individual person presents always unknown quantities. In the field of law there are many groups of cases in which the members are distinguishable by only relatively unimportant differences. It is in the courts that the practice of law most nearly resembles the practice of medicine. Here in a significant way is the growing point in law, which deals with the psychologic implications of individual and community motive, and reactions to environmental conditions.

The formal differences between preparation for medicine and for law in the statute lie chiefly in the additional school year required by the former. Another year as intern in an approved hospital is demanded by some schools before the conferring of the degree and in some states before the license to practice is granted. Many physicians spend more than one year in hospitals before entering independent practice. Thus the tendency is to extend the time difference between these two professions to two years.

The justification for these discrepancies in preparation lies in the inherent differences in the nature of the two fields of practice and the two kinds of knowledge required. Owing to the remarkable progress in science and its applications, there is in spite of much popularization, a greater discrepancy between the equipment of the general practitioner of medicine and the average educated man, than between that of the general practitioner of law and a correspondingly qualified product of our institutions of learning. Notwithstanding important studies and research in the history of law and some penetrating analyses with far-reaching results in the past seventy-five years, nothing has happened in law in that time which can be compared with the changes in the healing art. So great have been some changes in theory and practice that one is tempted to think of contemporary medicine as *new*, forgetting how old the new may be.

Through the progress of science in opening up vast fields of knowledge and pointing out even vaster fields where knowledge is not yet attained, through the developments of preventive medicine and the changing significance of the term "health", problems of almost appalling magnitude confront the physician. They are problems of science and of its application in art. But even if one recognizes the interdependence of kindred sciences and arts in promoting the welfare of mankind, the critical position is held by medicine. And so the generally accepted minimum requirements of two years in college and four years in the medical school are being left farther behind by what the average student of medicine actually and voluntarily requires of himself in preparation for his life work. Almost every year more holders of the baccalaureate degree receive the degrees in medicine. Few enter practice without a year's internship, although it is not generally required, and more than one year of internship is widely sought. It is true of both law and medicine, but especially of medicine, that the facts of practice demand more than is established in the formal standards set by the Bench and by statute.

We congratulate the Massachusetts Bar in the action taken in raising the standards for the education of the members of the legal profession.

What of medicine in Massachusetts? For many years the Board of Registration in Medicine has presented bills designed to require that medical students shall be given that preparation which is essential for the scientific practice of medicine. This education and training must be in the medical schools; nowhere else is it available. But this Commonwealth is indifferent respecting the right of a person to be assured that when he matriculates in a medical school he may be fitted to take his proper place in the ranks of those who are qualified to deal with the health of her people.

This attitude seems strange to the other States in the Union.

Does not the explanation of this fatuous attitude rest with the medical profession in large part? Every doctor in this State, who is qualified to teach our citizens their responsibility, should enroll in a campaign of education dedicated to the instruction of the electorate in the importance of well-trained practitioners of medicine. Until this is done the profession must bear a large part of the responsibility for this deplorable situation.

THE CLINICAL CONGRESS OF THE CONNECTICUT STATE MEDICAL SOCIETY

ONE of the important Clinical Congresses of the year, that of the Connecticut State Medical Society, will be held in New Haven, September 18, 19 and 20, 1934.

An invitation to attend this Congress was extended by the delegate from the Connecticut Medical Society at the Annual Meeting of the Massachusetts Medical Society.

A brief program, which presents the well-selected group of subjects to be considered, appears on page 287 of this issue.

The names of the authors of papers and of those who will participate in the discussions guarantee the excellence of the addresses. Taken as a whole, those who are in attendance will profit by valuable postgraduate instruction in up-to-date medicine. Members of the sister state societies should take advantage of these opportunities to see and hear many of the leading men in medicine in this country.

Our Connecticut brethren are gracious hosts. Time spent in attendance will be both valuable and highly enjoyable. Massachusetts should be well represented at these meetings.

A MATTER OF CONCERN TO THE MEDICAL PROFESSION

WHEN a prominent and respected physician is suspected of unethical conduct, much interest is aroused both in the professional and lay minds.

Considerable newspaper publicity relating to the affairs of Dr. Fred H. Albee of New York City, and Venice, Florida, has appeared setting forth that he has been suspended for a year by the Medical Society of the County of New York for alleged unprofessional advertising of the sanatorium in Venice, Florida, on the menus of a dining car. In the plea of Dr. Albee's counsel, as it is stated in the *New York Times*, Dr. Albee's photograph appears on the railroad advertising material.

Dr. Albee is reported to be the head of the sanatorium in question, and his defense is that after he had appealed to a railroad for better service to Venice, at the request of the railroad he furnished information about the sanatorium and its staff, but that the advertising material was composed, printed and distributed, without his knowledge or approval, and that upon learning of this menu he demanded its withdrawal. Dr. Albee's explanation that his position was confirmed by testimony of railroad officials in charge of this dining car service, was not effective in preventing action by the Society. The censors of the New York State Medical Society have upheld the action of the county society. Further action by the county society depends on an appeal by Dr. Albee to the Board of Delegates of the State Society which is the board of last resort. This Board of Delegates does not meet until after the suspension of Dr. Albee has expired; hence his suit in the supreme court with the purpose of securing a mandamus ordering the county society to reinstate him.

All of these alleged facts open the way for some discussion. If, as stated by Dr. Albee's counsel, his photograph appears on the railroad circular, one may wonder whether Dr. Albee provided this, and if he did, was he reasonably careful about its use, or at least worldly wise about some of the advantages of the physician's photograph in emphasizing the news value of publications.

Again since it does not appear that regret was expressed of any contributory negligence, and no public notice of the doctor's disapproval of the actions of the railroad, one may suspect that the county society felt driven to action.

That part of the defence which alleged that the action of the medical society was in response to a spirit of jealousy on the part of doctors practicing in another section of Florida seems puerile, for it is hardly supposable that the officers of the county and state society should use disciplinary measures without due cause.

However this unpleasant episode may terminate, one may feel concern if it is found that even the supreme court can regulate suspensions of members of a professional society. It is quite likely that a suit against a society for damages following unjust disciplinary action would have

standing in court, but to take from a society the right to suspend a member seems unreasonable. All of these proceedings are of interest, and it may be that this case will furnish useful lessons pertaining to behavior and the rights of medical societies.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

WAGNER, HARVEY S. Ph.B., M.D. University of Michigan Medical School 1903. Superintendent, Barnstable County Sanatorium. His subject is "Symptoms as a Measurement of Tuberculous Activity." Page 237. Address: Barnstable County Sanatorium, Pocasset, Massachusetts.

HUNT, FRANK H. M.D. University of Virginia Department of Medicine 1899. Resident Medical Officer at the Boston Sanatorium. Instructor at Harvard University. His subject is "Physical Signs as a Measure of Activity in Pulmonary Tuberculosis." Page 239. Address: Boston Sanatorium, Mattapan, Massachusetts.

PETTINGILL, OLIN S. M.D. Bowdoin Medical School 1908. Formerly Assistant Superintendent, Rhode Island State Sanatorium. Superintendent, Western Maine State Sanatorium. Now, Superintendent, Essex County Sanatorium. His subject is "The X-Ray in the Measurement of Activity in Pulmonary Tuberculosis." Page 240. Address: Essex County Sanatorium, Middleton, Massachusetts.

BADGER, THEODORE L. A.B., M.D. Harvard University Medical School 1926. Assistant in Medicine, Harvard Medical School. Research Fellow, Thorndike Memorial Laboratory, Boston City Hospital. Junior Visiting Physician, Boston City Hospital. Visiting Physician, Channing Home for Tuberculosis, Boston. Address: 264 Beacon Street, Boston, Massachusetts. Associated with him is

MYERS, WALTER K. B.S., M.D. Johns Hopkins University School of Medicine 1929. Resident Physician, Thorndike Memorial Laboratory, Boston City Hospital. Assistant in Medicine, Harvard Medical School. Address: Boston City Hospital, Boston. Their subject is "An Analysis of the Quantitative Tuberculin Test As An Index of Tuberculous Activity." Page 241.

KAMINSKY, JACOB. A.B., M.D. University of Nebraska College of Medicine 1923. Formerly, Assistant Physician, Rutland State Sanatorium. Now, Senior Physician, Middlesex County Sanatorium. Instructor in Tuberculosis, Boston University School of Medicine. His subject is "The Leucocytic Picture as an Aid in the Measurement of Activity in Pulmonary Tuberculosis." Page 245. Address: Middlesex County Sanatorium, 775 Trapelo Road, Waltham, Massachusetts.

MULLER, GULLI LINDH. A.B., M.D. College of Physicians and Surgeons, Columbia University, 1921. Formerly, Assistant Physician, Thorndike Memorial Laboratory, Boston City Hospital. Research Fellow in Medicine, Harvard Medical School. Now, Pathologist, Rutland State Sanatorium. Address: Rutland State Sanatorium, Rutland, Massachusetts. Associated with him is

DAVIDSON, DORIS L. A.B. Smith College 1918. Laboratory Assistant, Rutland State Sanatorium. Address: Rutland State Sanatorium, Rutland, Massachusetts. Their subject is "The Monocyte-Lymphocyte Ratio as a Measurement of Activity in Pulmonary Tuberculosis." Page 248.

CASS, JOHN W., JR. Ph.B., M.D. Yale University School of Medicine 1929. Assistant in Medicine, Massachusetts General Hospital. Physician, Channing Home. Address: 205 Beacon Street, Boston, Massachusetts. Associated with him is

SUTERMEISTER, MARGARET. B.S., C.P.H. Yale University 1931. Formerly, Research Assistant at University of Minnesota and Yale University. Address: 205 Beacon Street, Boston, Massachusetts. Their subject is "The Schilling Differential Count and Red Cell Sedimentation Rate as a Measurement of Activity in Pulmonary Tuberculosis." Page 252.

ORDWAY, WILLIAM H. M.D. Yale University School of Medicine 1914. Physician-in-Charge of the Metropolitan Life Insurance Company, Sanatorium. His subject is "Discussion and Summary of the Whole Problem with Especial Reference to the Study of the Leucocyte Count in Pulmonary Tuberculosis." Page 260. Address: Metropolitan Life Insurance Company Sanatorium, Mount McGregor, New York.

HAUBRICH, BERNARD P. B.S., M.D. Boston University School of Medicine 1927. On Staff of Claremont General Hospital. His subject is "Phenobarbital Poisoning." Page 264. Address: Claremont, New Hampshire.

TAYLOR, HERBERT L. M.D. Jefferson Medical College 1902. F.A.C.S. Consulting Surgeon, York Hospital, York, Maine. Member of the Staff, Portsmouth Hospital, Portsmouth, New Hampshire. His subject is "Bone Tumors." Page 267. Address: 160 Middle Street, Portsmouth, New Hampshire.

MACCHIA, BART F. M.D. Tufts College Medical School 1924. His subject is "Obstetrics in General Practice. A Review of 1,000 Cases." Page 273. Address: 4 Charter Street, Boston, Massachusetts.

CORRESPONDENCE

REPUDIATION OF A BOOK REVIEW

The publication of the letter appended below, by Dr. William J. Robinson, is in accordance with the policy of the *Journal* to be fair to the authors of books submitted for review in our columns. We assure Dr. Robinson that there was no personal animus in the mind of the reviewer.

Our Mysterious Life Glands

July 19, 1934.

Editor, *New England Journal of Medicine*,

A review of my book, "Our Mysterious Life Glands and How They Affect Us," has just been brought to my attention.

It is a thankless task to argue with reviewers, but when one makes statements that are manifestly unfair and untrue, then the author owes it to himself to protest.

Any unbiased reader would agree that your reviewer was motivated by personal animus. It is seen from the first line. In the first paragraph he speaks of my including the vitamins "for some inexplicable reason". Are endocrine secretions and the vitamins so absolutely separated by an impassable gulf that a book may not treat of the two, when it distinctly states on the title page that the book deals with both the internal secretions and the vitamins? Doesn't your reviewer know that many diseases are closely connected with the dysfunctions of the endocrine glands and deficient vitamins?

Your reviewer speaks of my book as "another horror in the form of a pseudo-scientific analysis of many disorders inferentially dependent upon endocrine dysfunction". He is entitled to his opinion, though I must say that not a single other medical journal has spoken in that vein of my book. A review appeared in the last issue of the *Journal of the American Medical Association*, and it is quite different from your reviewer's "review".

Your reviewer speaks of "many disorders *inferentially* dependent upon endocrine dysfunction". Is that an honest statement? What does he mean by "inferentially"? Are the various diseases I have treated of in my book not dependent upon endocrine dysfunction? Are cretinism, myxedema, exophthalmic goiter, acromegaly, gigantism, dwarfism, Addison's disease, etc., not dependent upon endocrine dysfunction?

As to my personal ideas of therapy, an honest reviewer would have honestly stated that I have been careful not to deal with hypotheses and with questionable preparations. I said distinctly that "the glandular preparations and their hormones are delicate substances . . . and the investigation and the decision must therefore be left to a competent and unbiased authority. The Council on Pharmacy and Chemistry of the American Medical Association is the highest authority we have in this country. I have, therefore, in mentioning glandular preparations and hormones that are used therapeutically, limited myself only to such as have been passed upon and approved by the before mentioned Council on Pharmacy and Chemistry".

I could have passed with silence some of his remarks, but I cannot remain silent when he says that the book should be relegated "to the class of pornography and charlatanism". I cannot pass over such a statement without the most vigorous protest.

For thirty-two years, since the foundation of *The Critic and Guide*, which has not missed a single issue under my sole editorship, I have been fighting charlatanism and pornography. One can easily see that I have never hesitated to fight quackery in medicine, quackery in and out of the profession, charlatanism in every form, and pornography under any mask. Again and again I called attention to the difference between scientific sexology and pornography, literary or pictorial. Never did I hesitate to fight dishonesty, oppression or tyranny, no matter where it showed its head, and regardless of the consequences. As a matter of fact many radicals consider me a prude or a Puritan, a conservative, or even a reactionary in sexual matters. And the sale of my books, because of their conservatism, their moderation, their fighting of pornography, is very much below that of ultra-radical sex books, many of which I consider purely pornographic.

Professor Maurice A. Bigelow, of Teachers' College and of the American Social Hygiene Association, knows that I have always been fighting pornography and commercial obscenity. John Rathbone Oliver, M.D., Ph.D., associate professor at Johns Hopkins University, in his book, "Psychiatry and Mental Health," has the following to say (on page 228). After referring to a number of my books he says: "I believe that there is no doubt of Dr. Robinson's sincerity. His productions are much the best of their type, and are not to be confounded with other books on similar subjects which are written and printed merely to sell and not to instruct."

I could point out hundreds of reviews, medical and lay, praising the *chastity* of the language of all my books, my opposition to anything that savors of pornography or obscenity or commercial sensationalism.

Nowhere at all does your reviewer try to point out my mistakes, my pseudo-scientific analysis or my pornography.

In view of the above, I think that you, yourself, Mr. Editor, will agree that the above referred to review was most unfair and was not motivated by objective truth but by personal animus.

Sincerely yours,

WILLIAM J. ROBINSON, M.D.
319 West 48th Street,
New York City.

RECENT DEATHS

GIRARDI — Victor Joseph Girardi, M.D., of 45 Highland Avenue, with an office at 57 Main Street, North Adams, Massachusetts, died August 2, 1934, by drowning. He was born in 1899 at Brescia, Italy, and came to this country at the age of six years. He formerly lived in Athol, Massachusetts, and received his M.D. degree in 1924 from the Harvard Medical School. He had served on the local school board. He is survived by his widow and a son.

NIELD — William Andrew Nield, M.D., of 286 Pleasant Street, New Bedford, Mass., died at the Massachusetts General Hospital, June 12, 1934, of coronary thrombosis.

He was born in Millbury, Mass., September 12, 1874, graduated in medicine from the Baltimore Medical College in 1902, and had practiced general medicine for thirty-two years. He was especially interested in tuberculosis and crippled children. He was the President of the Sol-e-Mar Hospital, where orthopedic service is maintained for children.

HORR — Albert Winslow Horr, M.D., of Malden, Massachusetts, formerly having an office at 419 Boylston Street, Boston, died at the home of his son in Watertown, New York. Announcement appeared in the Boston papers August 4, without specific date of death.

Dr. Horr was born in 1865 and graduated from the Boston University School of Medicine in 1891. He was former Professor of Ophthalmology at the Boston University School of Medicine and after retiring was made Professor Emeritus. He joined the Massachusetts Medical Society in 1919.

NIGRO—Michele Nigro, M.D., of 96 Forest Street, Medford, with an office at 270 Commonwealth Avenue, Boston, died at his home, August 3, 1934. He was born in Italy in 1882.

Dr. Nigro graduated from the Harvard Medical School in 1915 and joined the Massachusetts Medical Society in the same year. A widow, Madelyn Cuneo Nigro, two sons, two daughters, four brothers and a sister survive him.

NOTICE OF MEETING

TENTH CLINICAL CONGRESS OF THE CONNECTICUT STATE MEDICAL SOCIETY

New Haven, September 18, 19, 20, 1934

Changes have been made this year in general arrangements for the Clinical Congress.

The registration fee has been reduced to $2.00. Lunches are not included.

The evening dinner meetings have been omitted and the scientific program will be continued into the evenings of Tuesday and Wednesday.

A social hour to begin at 4:30 on each day of the congress has been arranged. County secretaries will serve as hosts.

Afternoon sessions each day will be devoted to demonstrations and round table discussions on the subjects that have been presented at the morning sessions.

Free parking of automobiles for members of the congress will be available nearby, and telephone service will be maintained. Members can be reached by calling New Haven 5-1161, Clinical Congress extension.

If you expect to attend the congress, please send your check for $2.00, made payable to the Connecticut Clinical Congress. Names and addresses of all who register before August 25 will be published in the final program. Apply to

Creighton Barker, M.D.,
Chairman of the Committee on Publicity and Registration.
129 Whitney Avenue, New Haven, Conn.

Tuesday, September 18

All times given are Daylight Saving Time

10:00 A.M.

Auditorium, Sterling Hall of Medicine

The Symptomatology, Diagnosis and Treatment of Lumbosacral and Sacroiliac Strain. Dr. George E. Bennett.

The Treatment of Arthritis from the Clinical Standpoint. Dr. Russell L. Cecil.

The Etiologic Theories and Therapeutic Trends in Chronic Arthritis. Dr. Robert B. Osgood.

A Discussion of the Diagnosis and Treatment of Some of the Common Disabilities Causing Pain in the Upper Extremity. Dr. Frank R. Ober.

2:30 P.M.

Brady Memorial Laboratory

Demonstrations and Round Table Conferences

Presentation of Cases Representing the Different Types of Arthritis from an Etiologic Standpoint. Dr. Denis S. O'Connor.

Anatomical and Pathological Demonstration of Shoulder Structures and Conditions. Dr. Edwin Pyle.

Motion Picture and Practical Demonstration of the New Hawley Fracture and X-Ray Table. Dr. George W. Hawley.

A Practical Demonstration of the Clinical Aspects of Back Pain. Dr. Paul P. Swett.

4:30 P.M.

Social Hour

Reception Room, Sterling Hall of Medicine

8:00 P.M.

Auditorium, Sterling Hall of Medicine

The Problem of Sudden Death: from the Pathological Standpoint. Dr. Harrison S. Martland.

The Problem of Sudden Death: from the Clinical Standpoint. Dr. Louis Hamman.

WEDNESDAY, SEPTEMBER 19

10:00 A.M.

Auditorium, Sterling Hall of Medicine

Diagnosis and Treatment of Some Common Skin Diseases. Dr. Howard Fox.

The Treatment of Pneumococcal Lobar Pneumonia, with Special Consideration of the Use of Antipneumococcus Serum and Artificial Pneumothorax. Dr. Francis G. Blake.

Gonorrhea in the Male and Its Treatment. Dr. P. S. Pelouze.

Pathogenesis of Pyuria in Early Life. Dr. Oscar M. Schloss.

2:30 P.M.

Brady Memorial Laboratory

Demonstrations and Round Table Conferences

Temperature Charts and Pathological Specimens of Malformations Having to do with Pyelitis in Children. Dr. Oscar M. Schloss, Dr. Howard W. Brayton, Dr. J. Harold Root and Dr. Oliver L. Stringfield.

Gonorrhea in the Male and Its Treatment. Dr. P. S. Pelouze.

Demonstration of Lobar Pneumonia. Dr. Francis G. Blake.

Demonstrations of

(a) The More Common Skin Diseases. Dr. Ralph E. McDonnell.

(b) Patch Test Method of Determining the Cause of Contact (Industrial) Dermatitis. Dr. Maurice J. Strauss.

Demonstrations of Problems of Sudden Death. Staff in Pathology.

4:30 P.M.

Social Hour

Reception Room, Sterling Hall of Medicine

8:00 P.M.

Auditorium, Sterling Hall of Medicine

The Importance of the Consideration of the Personality in General Practice. Dr. C. Macfie Campbell.

THURSDAY, SEPTEMBER 20

10:00 A. M.

Auditorium, Sterling Hall of Medicine

Psychoses Complicating Other Diseases. Dr. Alfred Stengel.

Prophylactic Vaccination. Dr. Stanhope Bayne-Jones.

Diagnosis of the Ordinary Endocrine Disorders. Dr. Max A. Goldzieher.

Therapeutic Uses of Parathormone. Dr. Alexander B. Gutman.

The Therapeutic Use of the Cortical Hormone of the Suprarenal Gland. Dr. Carl H. Greene.

Useful Endocrine Preparations in Gynecology. Dr. John Rock.

2:30 P.M.

Brady Memorial Laboratory

Demonstrations and Round Table Conferences

Clinical Presentation of Patients to Illustrate the Papers of Dr. C. Macfie Campbell and Dr. Alfred Stengel. Dr. Eugen Kahn.

Round Table Discussion to Consider the Practical Value of Various Endocrine Preparations on the Market and Methods of Administering Those of Proven Usefulness. Dr. John Rock.

Demonstration of Hyperparathyroidism. Dr. John P. Peters.

Demonstration of the Preparation and Effects of Some of the Materials Used for Prophylactic Vaccination. Dr. Stanhope Bayne-Jones.

Demonstration of Experimental Dogs Relieved of Diabetes by Removal of the Pituitary Gland. Dr. Harold E. Himwich.

Display of Wall Panels and Specimens Showing the Different Reactions to Testicular and Ovarian Hormones. Prof. Edgar Allen.

4:30 P.M.

Social Hour

Reception Room, Sterling Hall of Medicine

OFFICERS

Milton C. Winternitz, Chairman.
Herbert Thoms, Secretary.
Charles E. Sanford, Treasurer.
Walter R. Steiner, President of the Society.
J. Douglas Gold, Chairman of the Council.
Charles W. Comfort, Secretary of the Society.

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

August 18 - September 30—Medical Study Trip to Hungary. See page 975, issue of May 10.

September 3-6—American Public Health Association. at Pasadena, California. Dr. J. D. Dunshee, Chairman, Local Committee on Arrangements.

September 4, 5, 6—International Union Against Tuberculosis. For information address the National Tuberculosis Association, 450 Seventh Avenue, New York City.

September 10, 11, 12, and 13—American Congress on Physical Therapy will meet in Philadelphia at the Bellevue Stratford. For details write American Congress of Physical Therapy, 30 North Michigan Avenue, Chicago, Illinois.

September 10-15—First International Congress of Electro-Radio-Biology will be held in the Doges Palace at Venice. For details address the General Secretary of the Congress, Dr. Giocondo Protti, S. Gregorio 173, Venice (Italy).

September 18, 19 and 20—Tenth Clinical Congress of the Connecticut State Medical Society. See page 287.

September 27 and 28—International Association for Preventive Pediatrics will be held at Lyons. For details address the Secretary of the I. A. P. P., 15 rue Lévrier, Geneva (Switzerland).

September 28-29—New England Surgical Society will meet at Burlington, Vermont. For details address the Secretary, Dr. John M. Birnie, 14 Chestnut Street, Springfield, Mass.

October 22 - November 2—1934 Graduate Fortnight of the New York Academy of Medicine. See page 1240, issue of June 7.

October 31 - November 2—Massachusetts State Nurses' Association, Hotel Statler, Boston. For information write Miss Helene G. Lee, R.N., 420 Boylston Street, Boston.

April 29 - May 3, 1935—The American College of Physicians will meet in Philadelphia. For information address Mr. E. R. Loveland, Executive Secretary, 133-135 South 36th Street, Philadelphia, Pa.

June, 1935—Medical Library Association will meet in Rochester, N. Y. For details address the Secretary: Miss Frances N. A. Whitman, Librarian, Harvard University Schools of Medicine and Public Health, Boston, Mass.